

Protein Provision in Critically Ill Adults Requiring Enteral Nutrition: Are Guidelines Being Met?

Nutrition in Clinical Practice
Volume 34 Number 1
February 2019 123–130
© 2018 American Society for
Parenteral and Enteral Nutrition
DOI: 10.1002/ncp.10209
wileyonlinelibrary.com

WILEY

Alexandra Mitchell, RD, MClinRes^{1,2,*} ; Rowan Clemente, RD, BSc¹;
Claire Downer, RD, MSc¹; Frances Greer, RD, BSc¹; Kaylee Allan, RD, BSc¹;
Avril Collinson, RD, PhD²; and Stephen Taylor, RD, PhD¹ 

Abstract

Background: In a previous audit, 81% of enteral protein prescriptions failed to meet protein guidelines. To address this, a very high-protein enteral formula and protein supplements were introduced, and protein prescriptions were adjusted to account for nonnutrition energy sources displacing enteral formula. This follow-up audit compared protein provision in critically ill adults requiring exclusive enteral nutrition (EN), first, with local and international guidelines, and second, after changes to practice, with the previous audit in the same intensive care unit (ICU). **Methods:** Data were collected from 106 adults consecutively admitted to the ICU of a U.K. tertiary hospital and requiring exclusive EN ≥ 3 days. Protein targets based on local guidelines (1.25, 1.5, or 2.0 g/kg/d), nutrition prescription, and delivery were recorded for 24 hours between days 1–3, 5–7, 8–10, and 18–20 post-ICU admission. **Results:** The proportion of day 1–3 protein prescriptions meeting protein targets increased from 19% in 2015 to 69% in 2017 ($P < .0005$, $\phi = 0.50$). The median percentage of protein target delivered was lower than prescribed (79% vs 103%; ($P < .0005$; $r = 0.53$) and EN delivery only met the target of 22% of patients. The proportion of protein prescriptions meeting protein targets was similar for days 1–3 (69%), 5–7 (71%), and 8–10 (68%), but increased slightly by days 18–20 (74%). The proportion of patients for which EN delivery met protein targets increased with the number of days post-ICU admission (22%, 26%, 37%, and 53% for days 1–3, 5–7, 8–10, and 18–20, respectively). **Conclusion:** The proportion of protein prescriptions meeting guideline targets was higher after changes to practice. (*Nutr Clin Pract.* 2019;34:123–130)

Keywords

critical care; critical illness; dietary proteins; enteral nutrition; intensive care unit; nutrition assessment; nutrition support; quality improvement

Introduction

Catabolism of lean body mass during critical illness is associated with impaired immunity and wound healing, as well as weakness.^{1–4} Catabolism mobilizes energy substrates and

amino acids to maintain the acute-phase protein response.⁵ Nutrition, particularly protein, is key in attempting to minimize catabolism and maintain the acute-phase protein response during critical illness.⁵ Observational prospective cohort studies show an association between increased

From the ¹Department of Nutrition and Dietetics, Southmead Hospital, Bristol, United Kingdom; and ²Institute of Health and Community, University of Plymouth, Peninsula Allied Health Centre, Plymouth, Devon, United Kingdom.

*Present address: NIHR Bristol Biomedical Research Centre Nutrition Theme, University Hospitals Bristol Education & Research Centre, Upper Maudlin Street, Bristol BS2 8AE, United Kingdom

Financial disclosure: This audit was carried out and written up by A. Mitchell as a dissertation toward the award of master's in clinical research funded by the National Institute for Health Research.

Conflicts of interest: This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors. A. Mitchell and K. Allan have received speaker fees from Fresenius Kabi. The Department of Nutrition and Dietetics, North Bristol NHS Trust, on behalf of S. Taylor have received speaker and consultancy fees from Fresenius Kabi. North Bristol NHS Trust previously received funding from Nutrinovo for an earlier study. There was no commercial involvement in the study design, execution, analysis, or reporting of results. There is no other conflict of interest.

This article originally appeared online on November 19, 2018.

Corresponding Author:

Alexandra Mitchell, RD, MClinRes, NIHR Bristol Biomedical Research Centre Nutrition Theme, University Hospitals Bristol Education & Research Centre, Upper Maudlin Street, Bristol BS2 8AE, United Kingdom.
Email: alexandra.mitchell@bristol.ac.uk

Table 1. Local and International Guidelines for Protein Provision in Critically Ill Adults.

Guidelines	Protein, g/kg/d
Local trust guidelines	
CRP < 100 mg/L	1.25 ^a
CRP = 100–149 mg/L	1.5 ^a
CRP ≥ 150 mg/L	2.0 ^a
ESPEN guidelines (Singer et al, 2009) ¹¹	1.3–1.5 ^b
ASPEN guidelines (McClave et al, 2016) ¹⁰	1.2–2.5
Obese: BMI > 30 kg/m ²	2.0 ^b
BMI > 40 kg/m ²	2.5 ^b

ASPEN, American Society for Parenteral and Enteral Nutrition; BMI, body mass index; CRP, C-reactive protein; ESPEN, European Society for Clinical Nutrition and Metabolism; IBW, ideal body weight.

^aUse IBW if BMI > 25 kg/m².

^bUse IBW.

protein provision (≥ 1.2 g/kg/d) and improved clinical outcomes,^{6–8} but exact dose and timing have not been defined.⁹

Currently, for critically ill adults, the American Society for Parenteral and Enteral Nutrition (ASPEN) recommends 1.2–2.5 g/kg/d of protein and 2.0–2.5 g/kg ideal body weight (IBW)/d if body mass index (BMI) is > 30 kg/m².¹⁰ The European Society for Clinical Nutrition and Metabolism (ESPEN) recommends 1.3–1.5 g/kg IBW/d.¹¹ This compares with the Recommended Dietary Allowance for protein intake in healthy adults of 0.8 g/kg/d.¹²

It is difficult to achieve these goals without overfeeding energy¹³ because the nonprotein energy-to-nitrogen (NPE:gN) ratio of most enteral formulas and common use of nonnutrition energy (NNE) sources, such as propofol and citrate regional anticoagulation, are too high.¹⁴

Randomized controlled trials are required to define the effect of dose and timing of protein provision on clinical outcomes. However, we first need to establish how to provide high levels of protein without overfeeding energy.

There is a large deficit between protein guidelines vs prescription,¹⁴ and enteral/parenteral protein prescription vs delivery in intensive care units (ICUs) worldwide.^{15–17} In a previous audit in the study ICU, only 19% of enteral protein prescriptions met local guidelines.¹⁴ It was shown that, in theory, use of protein supplements and adjustment of protein prescriptions for NNE could significantly increase the proportion of patients meeting protein guidelines.¹⁴

As far as the authors are aware, no studies have compared both prescription and delivery of protein with guidelines in critically ill adults. Following up on the audit of enteral protein prescriptions reported by Taylor et al¹⁴ at the same ICU, this follow-up audit determines whether protein targets, based on guidelines (see Methods; Table 1), are met by enteral nutrition (EN) prescriptions and delivery since

implementing improvements in prescribing practice and EN products.

For the purpose of this study, nutrition prescription is defined as the total nutrition prescribed from enteral formula, supplements, and NNE sources per day. Nutrition delivery is the total nutrition actually provided to the patient from enteral formula, supplements, and NNE sources per day.

The aims of this study were: (1) to compare protein provision in critically ill adults who require exclusive EN (via feeding tube) with local and international guidelines; and (2) to provide a comparison with the previous audit of protein prescriptions in the same ICU following changes to practice.

Methods

Changes to Practice in EN Provision

Previous practice at the study ICU was for EN to be prescribed to meet the protein goal when no NNE was delivered. This meant that until NNE (usually propofol) stopped, EN was limited to prevent overfeeding; therefore, protein goals were often not met. The highest protein enteral formula available on the ICU was **Nutrison Protein Plus** (6.3 g protein, 14.2 g carbohydrate, 125 kcal/100 mL; NPE:gN 99:1; Nutricia, Wiltshire, United Kingdom). No protein supplements were stocked for use on the ICU.

Following the findings of the previous audit,¹⁴ where possible, dietitians prescribed EN to meet the full protein target, accounting for a reduced rate of enteral formula delivery because of the presence of propofol. This was facilitated by using a protein supplement (11 g protein, 1 g carbohydrate, 44 kcal/45 mL; **ProSource TF**; **Nutrinovo**, Kent, United Kingdom) and/or a very high-protein enteral formula (10 g protein, 12.9 g carbohydrate, 122 kcal/100 mL; NPE:gN 51:1; **Fresubin Intensive**; **Fresenius Kabi**, Cheshire, United Kingdom). Where the volume of enteral formula prescribed was less than the nutritionally complete volume, a soluble multivitamin was also prescribed to provide basic micronutrient requirements.

Participants

Adults (≥ 18 years old) admitted to the ICU of a tertiary hospital in the United Kingdom between April 22, 2017, and July 12, 2017, were included prospectively if they required exclusive EN on ICU admission. Exclusion criteria were exclusive EN no longer required or discontinued, or the patient discharged from ICU, within 72 hours of admission; patient not referred to the dietitian for EN within 72 hours of admission; clinical EN or protein restriction, for example, high refeeding risk, renal impairment requiring conservative management, liver dysfunction refractory to treatment,

or gastrointestinal (GI) dysfunction; parenteral nutrition (PN) indicated; oral nutrition commenced; or palliative care.

Data Collection

Patient characteristics were recorded on admission. Weight and height were taken from the patient's notes and were usually estimated or based on relatives' report or previous general practitioner's or hospital records.

Nutrition assessment and prescriptions were completed and reviewed daily Monday to Friday by experienced critical care dietitians. Resting metabolic rate, used to calculate estimated energy requirement (EER), was estimated using validated predictive equations for ventilated critically ill adults¹⁸ and nonventilated acutely ill adults,¹⁹ based on changing physiological parameters, as well as body weight. For nonventilated patients with burns, the validated Toronto equation was used when deemed most appropriate by the dietitian.²⁰

Dietitians estimated individualized protein targets based on local guidelines. Local and international guidelines for protein provision in critically ill adults are listed in Table 1. For patients with BMI >25 kg/m², an IBW equivalent to a BMI of 25 kg/m² was used when calculating protein targets using local guidelines. Local guidelines span most of the range recommended in the ASPEN guidelines, and therefore identifying whether protein prescriptions and delivery met protein targets based on local guidelines also shows whether ASPEN guidelines for protein provision can be met.¹⁰

Nutrition data were collected for 1 day during each of the following time periods in a patient's ICU stay: days 1–3, 5–7, 8–10, and 18–20. Day 1–3 of ICU stay were the primary data collection period, because protein prescriptions aimed to match the target from day 1, and all patients included required exclusive EN for ≥3 days. The first day audited for each patient was the first full day in the ICU after the patient had been assessed and target EN prescribed by a dietitian. The primary data collection period, day 1–3, matched that used in the 2015 audit, enabling direct comparison.¹⁴ Data collection was discontinued early if the patient no longer met the inclusion criteria.

Data were collated from patient dietetic records. Nutrition data collected were energy and protein targets based on local guidelines; equation used to calculate EER; reason for hypocaloric feeding, if appropriate; predicted and delivered NNE (propofol, intravenous [IV] glucose, citrate); nutrition prescription; enteral formula, supplements, and enteral fluid administered; and gastric residual volumes (GRVs) discarded or vomited. For patients undergoing continuous renal replacement therapy receiving citrate as anticoagulant in the continuous venovenous hemofiltration solution, it was assumed that they received an additional 200 kcal/d,

because it was not possible to determine individualized values.²¹

The protein prescription was calculated from the volume of enteral formula and supplements prescribed. Protein delivery was the amount of protein actually received by the patient in the enteral formula and supplements administered, minus gastric losses. In calculating nutrition delivery, gastric losses were accounted for to identify how much exogenous protein was received into the small intestine and was therefore available for absorption.

Nutrition Adequacy

Nutrition adequacy criteria were defined as ≥90% of the protein target and ≥130 g/d of carbohydrate (obligatory glucose requirement)¹² without overfeeding energy (≤100% EER), as used in the 2015 audit.¹⁴ The protein supplement provides protein in increments of 11 g, and therefore prescriptions could rarely achieve exactly 100% of protein target. The number of protein supplements prescribed was rounded down, and therefore the value of ≥90% of protein target was chosen to match protein goals associated with improved clinical outcomes in mechanically ventilated, critically ill adults (>90% of 1.2–1.5 g/kg/d or based on nitrogen balance).⁸ It was assumed this optimizes protein utilization, minimizing reliance on gluconeogenesis of amino acids and glycerol.¹⁴ The final adequacy criteria required that energy from all sources was ≤100% of EER, to avoid consequences of overfeeding^{22,23}; obese patients received hypocaloric prescription, well below 100% of EER, but with adequate protein to minimize catabolism.^{10,24} Results from analyses considering nutrition adequacy can be found in the supplementary material (Table S1).

Statistical Analyses

Variables were assessed for normal distribution using Q-Q plots and the Shapiro-Wilk test. Continuous variables that were normally distributed are described as mean ± SD. Nonnormally distributed continuous variables are described as median with interquartile range (IQR). Categorical variables are described as a percentage.

Fisher exact test was used to compare the proportion of protein prescriptions meeting protein targets based on local guidelines in the current audit with the 2015 audit,¹⁴ and ϕ was calculated to identify effect size. Wilcoxon signed rank test, with calculation of effect size r , was used to compare the difference between protein targets and protein prescriptions, and protein targets and protein delivery. Wilcoxon signed rank test was also used to compare the difference in the percentage of protein target met by prescription vs the percentage of protein target met by delivery. Continuous variables were compared between the 2015 and 2017 samples using the Mann-Whitney U test, with calculation of effect size r . The Mann-Whitney U test

Table 2. Comparison of Baseline Characteristics Between 2015 and 2017.

Characteristics	2015 (Taylor et al, 2016) ¹⁴ (n = 139)	2017 (n = 106)	P-Value
Mean age ± SD, y	59 ± 18	58 ± 17	.532
Sex male, n (%)	84 (60)	54 (51)	.154
Weight, median (IQR), kg	75.4 (65.0–88.0)	75.5 (64.9–89.6)	.841
BMI, median (IQR), kg/m ²	24.9 (22.6–28.7)	25.4 (22.5–28.7)	.768
APACHE II score, median (IQR)	17 (13–23)	16 (11–22)	.359
Diagnosis category, n (%)			.406
Trauma	41 (29)	38 (36)	
Neurosurgery (nontrauma)	29 (21)	27 (26)	
Surgery (other)	15 (11)	9 (9)	
Medical	54 (39)	32 (30)	

APACHE II, Acute Physiology and Chronic Health Evaluation II; BMI, body mass index; IQR, interquartile range.

Table 3. 2017 Protein Targets Based on Local Guidelines.

Days Post-ICU Admission	Protein Target, n (%)			Patients, n (%)
	1.25 g/kg BW ^a /d	1.5 g/kg BW ^a /d	2.0 g/kg BW ^a /d	
1–3	63 (59)	19 (18)	24 (23)	106 (100)
5–7	28 (43)	14 (22)	23 (35)	65 (61)
8–10	22 (58)	6 (16)	10 (26)	38 (36)
18–20	16 (84)	1 (5)	2 (11)	19 (18)

BMI, body mass index; BW, body weight; ICU, intensive care unit.

^aIdeal body weight used if BMI > 25 kg/m².

was also used to compare continuous variables in subgroup analysis. Categorical variables were compared between the same independent samples using Fisher exact test with ϕ or Cramer V reported as effect size, as appropriate. Subgroup analysis compared groups based on previously identified risk factors for failing to achieve protein targets.¹⁴ All statistical tests performed were 2-tailed. Magnitude of effect sizes was determined based on Cohen's²⁵ guidelines: 0.1 = small, 0.3 = medium, 0.5 = large.

Guidance from the National Audit Office suggests that a sample size of 100 is sufficient for most audit purposes.²⁶ A sample of 106 patients was included in the primary analyses for day 1–3 post-ICU admission. A retrospective sample size calculation showed that for the proportion of the sample identified as achieving the standard (protein targets based on local guidelines) with protein prescription and protein delivery, and with this sample size of 106 patients, accuracy was approximately ±8% with a confidence level of 95%.²⁷

Ethics

This project was accepted and registered as an audit by the local National Health Service (NHS) Trust and the university to which the authors were affiliated. NHS ethics approval was not required because all audit data were routinely collected for clinical purposes.

Results

Sample Characteristics

A total of 106 ICU patients requiring exclusive EN were included (Table 2). The majority of patients had a protein target of 1.25 g/kg/d based on local guidelines (Table 3). Baseline characteristics of patients included in the 2015¹⁴ and 2017 audits were similar (Table 2). The large proportion of trauma and neurosurgery patients reflects the hospital being a regional major trauma center.

Protein Prescription and Delivery Compared With Guidelines

The proportion of protein prescriptions meeting protein targets based on local guidelines on day 1–3 of ICU admission increased from 19% (n = 27/139) in 2015 to 69% (n = 73/106) in 2017, with large effect size ($P < .0005$; $\phi = 0.50$).

A higher percentage of patients' protein target was prescribed in 2017 compared with 2015 (median 103% [IQR 97%–108%] vs 75% [IQR 62–95]; $P < .0005$; $r = 0.54$: large effect size). In the 2017 audit, 99% (105/106) of protein prescriptions achieved >75% of their protein target with prescription, the median proportion achieved in the 2015 audit. Protein targets in 2015 were slightly higher than in 2017 (median 108.3 [IQR 84.4–129.2] vs

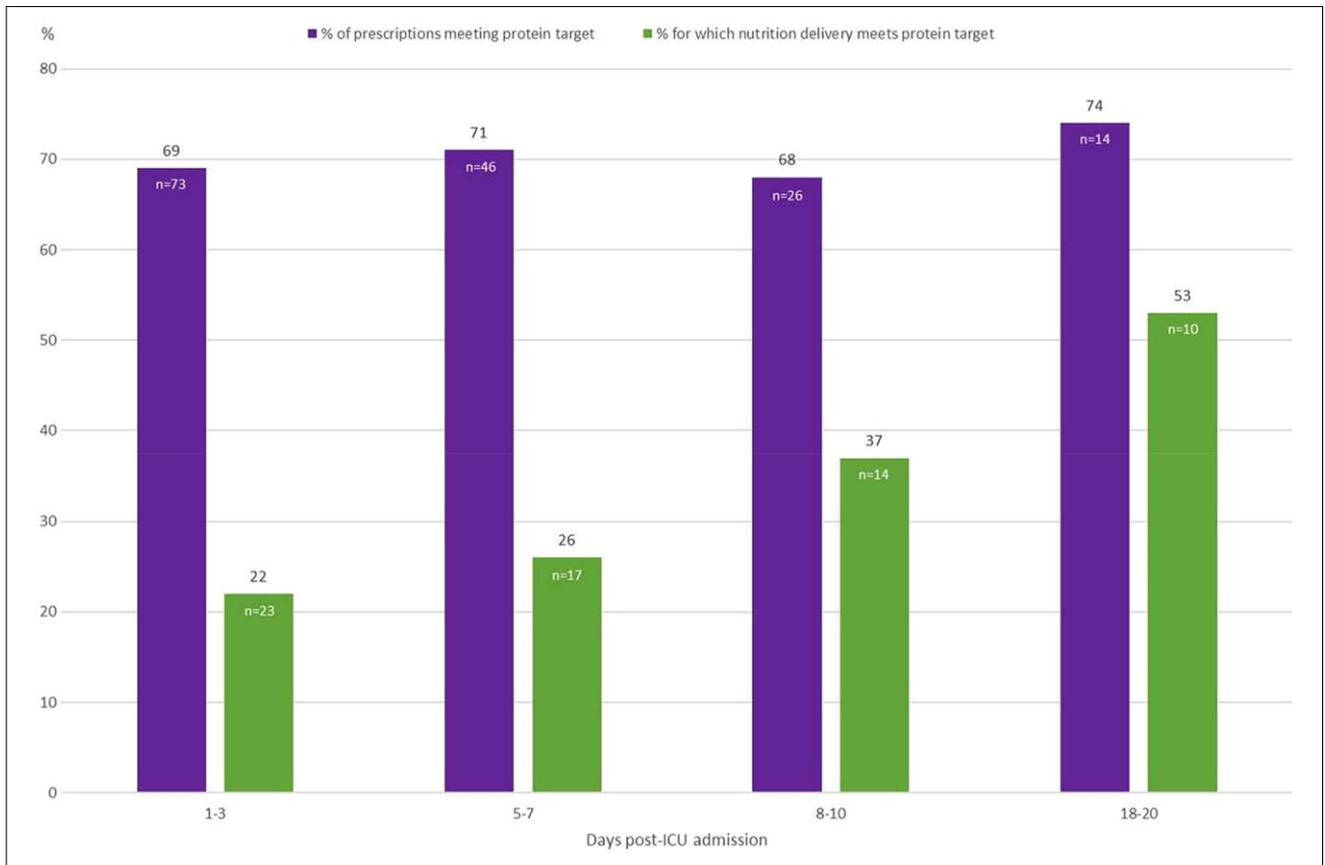


Figure 1. Percentage of patients achieving protein targets with nutrition prescription and delivery.

97.2 [IQR 84.0–116.4] g/d; $P = .135$, $r = 0.09$: small effect size; normalized: median 1.32 [IQR 1.10–1.88] vs 1.25 [IQR 1.17–1.50] g/kg/d).

Figure 1 shows a comparison over time between the percentage of protein prescriptions meeting protein targets based on local guidelines and the percentage of patients meeting protein targets with EN delivery.

The median protein prescription on day 1–3 was 3 g higher than the protein target, but not of clinical significance. Protein delivery on day 1–3 was lower than protein target (median 79 vs 97 g; $z = -6.89$; $P < .0005$; $r = 0.47$: medium-to-large effect size) with the difference of 18 g between median protein target and delivery being potentially clinically significant (Figure 2). Median percentage of protein target met by delivery on day 1–3 was 79% vs 103% for the percentage of protein target met by prescription ($z = -7.70$; $P < .0005$; $r = 0.53$: large effect size).

Complete data for energy and protein targets, prescription, and delivery can be found in Table S2.

Risk Factors for Inadequate EN

Patients with the highest protein target, 2.0 g/kg/d, were less likely to meet their protein target with prescription

(46% vs 79% and 75% for targets of 2.0, 1.5, and 1.25 g/kg/d, respectively; $P = .027$, Cramer V = 0.27: medium effect size). For delivery, there was a trend in the same direction (12% vs 21% and 25% for targets of 2.0, 1.5 and 1.25 g/kg/d, respectively; $P = .489$, Cramer V = 0.13: small effect size).

Patients prescribed hypocaloric nutrition because of obesity or metabolic intolerance were more likely to meet their protein target with prescription (84% vs 66%; $P = .171$; $\phi = 0.155$: small effect size). The same analysis could not be done for delivery because of insufficient numbers in some groups.

For delivery, NNE as a percentage of total energy was higher in the group that failed to meet their protein target compared with those who met their protein targets (median 10% [IQR 0%–23%] vs 6% [IQR 0%–9%]; $U = 680$; $z = -1.922$; $P = .055$; $r = 0.19$: small effect size).

Discussion

Changes in prescribing practices, made in response to the 2015 audit,¹⁴ were associated with more protein prescriptions meeting protein targets based on local guidelines, increasing from 19% (2015) to 69% (2017); the slightly lower

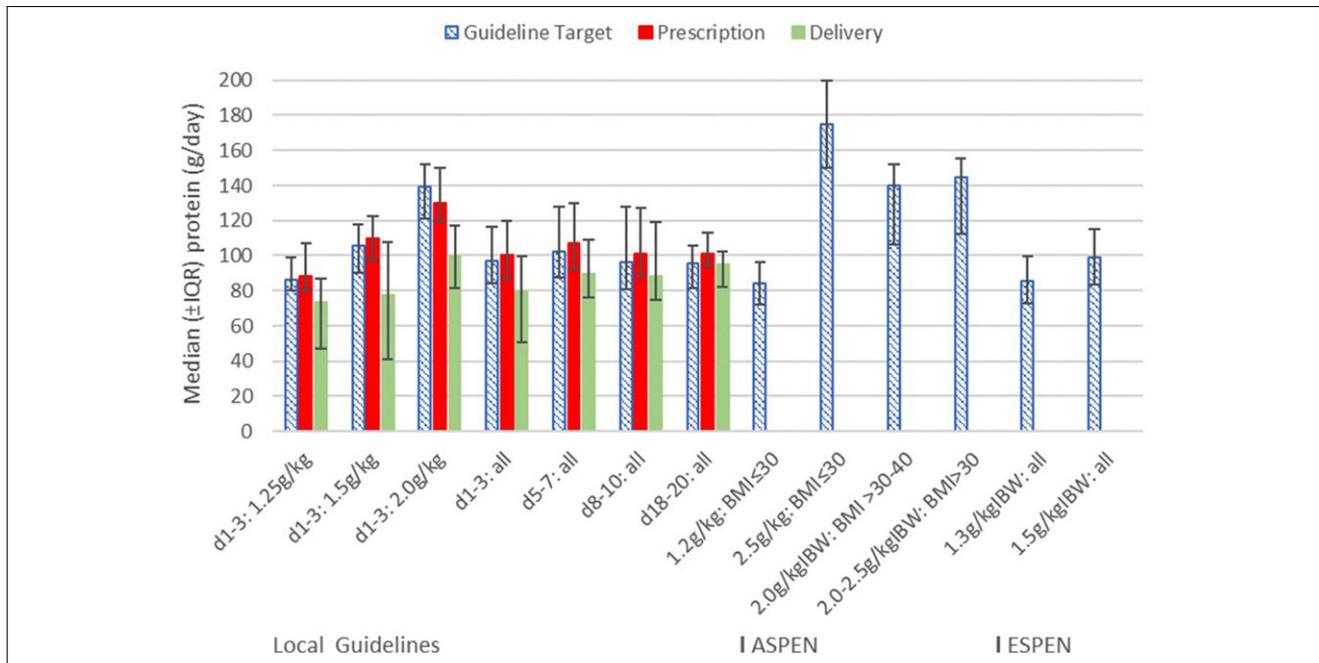


Figure 2. Protein targets based on local and international guidelines compared with prescription and delivery. Target is calculated daily requirement based on guidelines; prescription is prescribed nutrition from enteral feed, supplements, and nonnutrition energy (NNE); and delivery represents actual nutrition received from enteral feed, supplements, and NNE. ASPEN, American Society for Parenteral and Enteral Nutrition; BMI, body mass index (kg/m^2); d, day post-ICU admission; ESPEN, European Society for Clinical Nutrition and Metabolism; IBW, ideal body weight; IQR, interquartile range.

protein targets in 2017 are unlikely to have contributed significantly.

The proportion of protein prescriptions meeting targets was similar over the first 10 days of ICU admission (68%–71%) with a small increase by day 18–20 (74%). It is likely that this was partly due to a reduced proportion of patients with higher protein targets (1.5 or 2.0 g/kg/d) at day 18–20 and a reduction in NNE permitting easier attainment of protein targets without overfeeding.

There was a trend for protein targets not to be met by prescriptions in patients with the highest protein targets (2.0 g/kg/d). At the time of this follow-up audit, dietitians tended to round down the number of protein supplements prescribed, making it more likely that patients would be slightly underprescribed rather than overprescribed protein. Due to the common underdelivery of EN, it may be beneficial to encourage dietitians to round up the number of supplements. Patients with high BMI, and therefore requiring hypocaloric feeding, were at increased risk for not meeting protein targets and the obligatory glucose requirement in the 2015 audit,¹² but not in the follow-up audit.

As seen in previous studies, there was a large gap between protein prescription and delivery.^{15,16} Only 22% of patients actually received their protein target on day 1–3, but this increased to 53% by day 18–20. Median percent of protein

target met by EN delivery, on day 1–3 of ICU admission, was 79% (IQR 54%–99%) compared with 103% (IQR 97%–109%) with prescription. Whereas the prescription IQR was narrow and straddled 100%, the IQR for delivery was wide and <100%, showing that nonprescription factors impair the meeting of targets. These factors were not investigated in this study but have been reported elsewhere to commonly include delays for tests and procedures, GI intolerance, and feeding tube problems.²⁸ Improvement in EN delivery with number of days post-ICU admission has also previously been described⁷ and is likely due to improvements in GI tolerance and reduced delays for procedures.²⁸

Further research is needed to investigate ways to improve EN delivery. Specifically, issues with enteral access and GI intolerance that limit EN delivery need to be investigated. We need to identify safe and effective solutions to reduce the frequency and severity of these problems or to provide alternative methods for delivering EN that bypass these issues. Where EN prescriptions still fail to meet requirements in some cases, specific clinical reasons such as biochemical abnormalities and organ dysfunction need to be investigated.

High NNE provision was the main risk factor for failing to meet protein target with EN delivery on days 1–3. Protein prescriptions were adjusted for predicted NNE, but when NNE delivery was higher than predicted, enteral formula

and therefore protein delivery would be reduced, preventing protein target being met. Raising awareness of the impact of NNE sources on patients' nutrition among the ICU multidisciplinary team is important to facilitate changes that may be implemented to reduce the amount of NNE, for example, changing type and/or dose of sedatives and IV fluids/solutions.

Local protein guidelines (1.25, 1.5, or 2.0 g/kg/d based on C-reactive protein [CRP] level) span most of the range recommended by ASPEN (1.2–2.5 g/kg/d); therefore, the factors suggested to affect protein prescription and delivery should largely apply to protein targets based on ASPEN guidelines.¹⁰ Lack of objective criteria for choosing an individual's protein target risk arbitrary choice between 1.2 and 2.5 g/kg/d; to avoid this, local guidelines match target to CRP level based on the consensus that higher input is of benefit in more severe illness.

The current and previous audit carried out on the same ICU¹⁴ are the only studies that have directly compared protein prescription with guideline targets. The most recent published data from the International Nutrition Survey (INS) report protein adequacy (percent of prescription met by delivery) for artificial nutrition (EN and PN) of 57.6% for all countries and 69.8% for Europe and South Africa.¹⁶ In the current audit, median percentage of protein target achieved with EN delivery was 79% and 102% on days 1–3 and 18–20, respectively.

The relative improvement of the current audit over INS results may be even larger because of differences in the way that data were collected and analyzed. Although most INS patients were prescribed EN, delivery for those receiving PN was likely to be closer to prescription.^{15,16} Mean protein prescription (\pm SD) was 1.2 g/kg/d (\pm 0.3) in the INS¹⁶ compared with higher and harder to attain protein targets of 1.25–2.0 g/kg/d in this audit. In this audit, EN delivery was adjusted for gastric losses, providing a more valid measure of the nutrition available to the patient for absorption. In contrast, exclusion of patients commencing partial oral intake from the current audit may have contributed to higher reported delivery in comparison with the INS.

A retrospective U.S. audit recorded protein adequacy from EN at day 3 of ICU admission, providing a similar comparison with day 1–3 delivery in the current audit.¹⁷ Protein adequacy was only 17% for the U.S. sample of mostly medical ICU patients.¹⁷ The current audit was at a major trauma center, and therefore included a large proportion of trauma and neurosurgery patients. In the U.S. audit, only 9% of patients audited received \geq 80% of their protein prescription on day 3, compared with 22% of patients in the current audit who received 100% of their protein target based on local guidelines, on day 1–3 of ICU admission.¹⁷

Prospective cohort studies carried out in the Netherlands reported a higher proportion of patients achieving their

protein target with EN delivery.^{6,29} Weijs et al⁶ reported that 30% of patients achieved at least 1.2 g/kg/d during the period of mechanical ventilation when targets were set at 1.2–1.5 g/kg/d. This is higher than the current audit on day 1–3 (22%), but by day 18–20, 53% met their protein target and these targets were higher (1.25–2.0 g/kg/d) and therefore more difficult to achieve.

The findings of the current audit, and other literature in this area, indicate that it is important for ICUs to audit their EN prescriptions and delivery to identify potential deficits. Based on this follow-up audit, it is suggested that protein deficits may be reduced significantly by the availability of a very high-protein enteral formula and an enteral protein supplement. Consideration of the displacement of EN by NNE sources such as propofol is important, particularly early in a patient's ICU stay, and protein prescriptions should be adjusted accordingly.

Prescribing adequate protein without overfeeding energy or restricting other nutrients such as carbohydrate, electrolytes, and micronutrients is a difficult balancing act. The ability to prescribe (and potentially therefore deliver) a balance of EN that is optimal for the critically ill patient is more likely to be achieved when the prescriber has access to both a range of enteral formulas that includes one with a low NPE:gN ratio and protein supplements easily administered via an enteral feeding tube. Further education of dietitians, physicians, and nurses is required to increase awareness of the potential for large nutrition deficiencies in ICU patients and changes they can make toward optimal prescribing and delivery of EN.

A limitation in this audit was the use of estimated or reported admission weight where no recent actual weight had been recorded. This represents a source of error in calculations of BMI, EER, and protein targets. However, use of estimated or reported weights reflects real-world circumstances where accurate current weights are rarely available for critically ill patients.

In calculating EN delivery, the assumption that all GRV loss was enteral formula or fluid will underestimate input because of unmeasurable dilution by saliva or gastric juice. In addition, when using a nasointestinal tube, it was assumed that if EN appeared in the GRV it meant all nasointestinal EN was really gastric; this may overestimate loss. Currently, there is no clinical method of more accurately accounting for GRV loss, but to ignore it would overestimate the percentage of target met.

Another limitation is the small sample size available for the days 8–10 and 18–20 analysis due to the large number of patients meeting exclusion criteria by this point in their ICU stay. Larger patient numbers and testing of this protocol in other centers are required to determine whether the results are generalizable.

In conclusion, a larger proportion of ICU EN prescriptions and delivery met their protein targets using protein

supplements and a low NPE:gN ratio enteral formula (51:1) with protein prescriptions adjusted to the current NNE input vs previous practice of adjusting protein prescriptions to 0 NNE and using NPE:gN ratio enteral formulas $\geq 99:1$. It is therefore recommended that where patients require low NPE:gN ratios, enteral formula with a similar NPE:gN ratio and/or protein supplements should be stocked.

Acknowledgments

We are grateful to Natalie Dumont, Jennifer Dacombe, Carolyn Power, Naomi Cassidy, and Stephanie Saker for their assistance with data acquisition.

Statement of Authorship

A. Mitchell and S. Taylor contributed to the conception and design of the research; A. Collinson contributed to the design of the research; A. Mitchell contributed to the acquisition, analysis, and interpretation of the data; S. Taylor contributed to the acquisition and interpretation of the data; R. Clemente, C. Downer, F. Greer, and K. Allan contributed to the acquisition of the data; A. Mitchell and S. Taylor drafted the manuscript. All authors critically revised the manuscript, agree to be fully accountable for ensuring the integrity and accuracy of the work, and read and approved the final manuscript.

Supplementary Information

Additional supporting information may be found online in the Supporting Information section at the end of the article.

References

- Batt J, dos Santos CC, Cameron JI, Herridge MS. Intensive care unit-acquired weakness: clinical phenotypes and molecular mechanisms. *Am J Respir Crit Care Med*. 2013;187(3):238-246.
- Puthuchery ZA, Rawal J, McPhail M, et al. Acute skeletal muscle wasting in critical illness. *J Am Med Assoc*. 2013;310(15):1591-1600.
- Watters JM, Bessey PQ, Dinarello CA, Wolff SM, Wilmore DW. Both inflammatory and endocrine mediators stimulate host responses to sepsis. *Arch Surg*. 1986;121(2):179-190.
- Meyer NA, Muller MJ, Herndon DN. Nutrient support of the healing wound. *New Horiz*. 1994;2(2):202-214.
- Hoffer LJ, Bistran BR. Nutrition in critical illness: a current conundrum [version 1; referees: 2 approved]. *F1000Research*. 2016;5(F1000 Faculty Rev):2531.
- Weijs PJM, Stapel SN, de Groot SDW, et al. Optimal protein and energy nutrition decreases mortality in mechanically ventilated, critically ill patients: a prospective observational cohort study. *JPEN J Parenter Enteral Nutr*. 2012;36(1):60-68.
- Nicolo M, Heyland DK, Chittams J, Sammarco T, Compher C. Clinical outcomes related to protein delivery in a critically ill population. *JPEN J Parenter Enteral Nutr*. 2015;40(1):45-51.
- Song JH, Lee HS, Kim SY, et al. The influence of protein provision in the early phase of intensive care on clinical outcomes for critically ill patients on mechanical ventilation. *Asia Pac J Clin Nutr*. 2017;26(2):234-240.
- Liebau F, Norberg Å, Rooyackers O. Does feeding induce maximal stimulation of protein balance? *Curr Opin Clin Nutr Metab Care*. 2016;19(2):120-124.
- McClave SA, Taylor BE, Martindale RG, et al. Guidelines for the provision and assessment of nutrition support therapy in the adult critically ill patient: Society of Critical Care Medicine (SCCM) and American Society for Parenteral and Enteral Nutrition (A.S.P.E.N.). *JPEN J Parenter Enteral Nutr*. 2016;40(2):159-211.
- Singer P, Berger MM, Van den Berghe G, et al. ESPEN guidelines on parenteral nutrition: intensive care. *Clin Nutr*. 2009;28(4):387-400.
- Institute of Medicine. Dietary reference intakes for energy, carbohydrate, fiber, fat, fatty acids, cholesterol, protein, and amino acids. Washington DC: National Academy Press; 2005.
- Jeejeebhoy KN. Permissive underfeeding of the critically ill patient. *Nutr Clin Pract*. 2004;19(5):477-480.
- Taylor S, Dumont N, Clemente R, Allan K, Downer C, Mitchell A. Critical care: meeting protein requirements without overfeeding energy. *Clin Nutr ESPEN*. 2016;11:e55-e62.
- Cahill NE, Dhaliwal R, Day AG, Jiang X, Heyland DK. Nutrition therapy in the critical care setting: What is "best achievable" practice? An international multicenter observational study. *Crit Care Med*. 2010;38(2):395-401.
- Heyland DK, Dhaliwal R, Wang M, Day AG. The prevalence of iatrogenic underfeeding in the nutritionally 'at-risk' critically ill patient: Results of an international, multicenter, prospective study. *Clin Nutr*. 2015;34(4):659-666.
- Stewart ML, Biddle M, Thomas T. Evaluation of current feeding practices in the critically ill: a retrospective chart review. *Intensive Crit Care Nurs*. 2017;38:24-30.
- Frankenfield DC, Coleman A, Alam S, Cooney RN. Analysis of estimation methods for resting metabolic rate in critically ill adults. *JPEN J Parenter Enteral Nutr*. 2009;33(1):27-36.
- Frankenfield DC, Ashcraft CM. Toward the development of predictive equations for resting metabolic rate in acutely ill spontaneously breathing patients. *JPEN J Parenter Enteral Nutr*. 2017;41(7):1155-1161.
- Allard JP, Pichard C, Hoshino E, et al. Validation of a new formula for calculating the energy requirements of burn patients. *JPEN J Parenter Enteral Nutr*. 1990;14(2):115-118.
- Oudemans-van Straaten HM, Ostermann M. Bench-to-bedside review: citrate for continuous renal replacement therapy, from science to practice. *Crit Care*. 2012;16(6):249.
- Weijs PJM, Looijaard WGPM, Beishuizen A, Girbes ARJ, Oudemans-van Straaten HM. Early high protein intake is associated with low mortality and energy overfeeding with high mortality in non-septic mechanically ventilated critically ill patients. *Crit Care*. 2014;18(6):701.
- Preiser JC, van Zanten ARH, Berger MM, et al. Metabolic and nutritional support of critically ill patients: consensus and controversies. *Crit Care*. 2015;19(1):35.
- Dickerson RN, Patel JJ, McClain CJ. Protein and calorie requirements associated with the presence of obesity. *Nutr Clin Pract*. 2017;32(1 suppl):86S-93S.
- Cohen J. Statistical power analysis for the behavioural sciences. 2nd ed. Hillsdale, NJ: Erlbaum; 1988.
- National Audit Office. *A Practical Guide to Sampling*. London: National Audit Office; 2006. <https://www.nao.org.uk/wp-content/uploads/2001/06/SamplingGuide.pdf>
- Ferday S. *An Introduction to Statistics for Local Clinical Audit and Improvement*. London: Healthcare Quality Improvement Partnership; 2015.
- Kim H, Stotts NA, Froelicher ES, Engler MM, Porter C. Why patients in critical care do not receive adequate enteral nutrition? A review of the literature. *J Crit Care*. 2012;27(6):702-713.
- Strack van Schijndel RJM, Weijs PJM, Koopmans RH, Sauerwein HP, Beishuizen A, Girbes ARJ. Optimal nutrition during the period of mechanical ventilation decreases mortality in critically ill, long-term acute female patients: a prospective observational cohort study. *Crit Care*. 2009;13(4):1-11.