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Considerations When Using Predictive Equations to Estimate Energy Needs Among Older, Hospitalized Patients: A Narrative Review

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Abstract
Purpose of Review The aim of this narrative review was to summarize the accuracy of predictive equations used to estimate energy expenditure in older, hospitalized adults.
Recent Findings More than 50% of patients admitted to intensive care units are older adults. Currently accepted prediction equations used to determine energy intake in the older, hospitalized patient were not specifically developed for the aging population. Rates of multimorbidity, polypharmacy, and malnutrition, conditions that influence energy expenditure, are higher in older adults compared to younger adults.
Summary For these reasons, current equations may not accurately assess energy needs in this population. As the evidence demonstrating the importance of nutritional supplementation in older, hospitalized adults grows, more accurate energy assessment methods that account for age-related conditions are needed to predict nutritional requirements.

Keywords Aging · Hospitalization · Critical illness · Enteral nutrition · Energy expenditure · Multimorbidity · Energy intake · Older adults

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Introduction

One in seven Americans is ≥65 years of age, a population expected to double over the next four decades [1]. Older patients have higher health care utilization, in addition to a greater chance of hospitalization compared to younger adults due to a greater number of comorbidities, less physiologic reserve, and lower premorbid functioning [2, 3]. Furthermore, the majority of older adults have at least one chronic condition [4, 5], which may lead to a greater susceptibility of hospital-acquired infections and other complications that further contributes to decline in function [6]. Malnutrition is also a prevalent issue within the health care setting that can contribute to functional decline [7], yet estimates suggest only half of malnourished patients are recognized and treated [8••, 9]. In order to appropriately inform nutrition recommendations, an accurate assessment of a patient's energy needs is required.

The determination of energy expenditure to prescribe caloric intake in hospitalized patients is a widely established medical practice [10]. Suboptimal levels of feeding are associated with poor clinical outcomes including poor wound healing, higher complication rates, and increased mortality [11–15]. Conversely, excess energy intake is associated with longer duration of mechanical ventilation, prolonged ICU admission, and increased overall length of stay [16]. Additionally, critical illness is considered a hypermetabolic state associated with increased protein catabolism [17], which suggests that current accepted formulas may yield inaccurate estimations of energy needs. Given the complications associated with over- or under-feeding as well as the higher healthcare utilization rates of the older population, accurate assessment of energy needs is critical in older people for targeted nutrition support. This review will focus on the current methods used to determine energy needs in hospitalized older adults and factors that should be considered when utilizing these methods.

Methods of Nutrition Assessment

Traditional methods of nutrition assessment are limited in the hospital and critical care setting. Diet history is usually difficult to determine or cannot be obtained due to severe injury. Weight measurements may be inaccurate due to fluid resuscitation, and abnormal values of serum or plasma proteins (albumin, transthyretin) may be influenced by the inflammatory state and severity of disease [18]. For these reasons, the American Society for Parenteral and Enteral Nutrition (ASPEN) and the Society of Critical Care Medicine (SCCM) recommend using indirect calorimetry, published predictive equations, or weight-based formulas to determine energy requirements [10].

Indirect calorimetry, considered the gold standard to estimate energy needs, is a method for which measurements of oxygen consumption and carbon dioxide are used to calculate resting energy expenditure (REE). However, indirect calorimetry is time-consuming and resource intensive, and specific training is required to operate systems. In addition, some clinical conditions impact resting energy expenditure measurements when obtained by indirect calorimetry [19]. In critically ill, mechanically ventilated patients, conditions that influence calorimetric measurement errors include hemodynamic or respiratory instability, variations of the carbon dioxide pool, intravenous carbohydrate load >15 kcal/kg/day, respiratory system air leaks, accumulation of intermediate metabolites, and high values of inspired oxygen fraction [19]. Due to these factors, energy needs are often estimated in the clinical setting using equations which are based on calculation of resting metabolic rate.

Currently accepted prediction equations exist as a low-cost alternative to measuring REE, commonly used equations include the Harris-Benedict equation, Mifflin-St. Jeor equation, Ireton-Jones equations, and weight-based equations that calculate calories per kilogram. A summary of published predictive equations is presented in Table 1. The Harris-Benedict and Mifflin-St. Jeor equations incorporate patient's height, age, and gender [24]. Likewise, the Penn State and Swinamer equations have been used specifically in critically ill patients and include factors such as ventilation rate and core temperature which may further influence energy expenditure. However, caution regarding the use of these prediction equations is warranted due to underrepresentation in most validation studies of older adult, critically ill, and racially diverse populations, all of whom may differ physiologically due to acute illness or chronic organ insufficiency [24]. Underestimations in energy expenditure for these equations ranged from 18 to 27%, while overestimations ranged from 5 to 12%. The Mifflin-St. Jeor equation, alternately, had the strongest performance in healthy, nonobese adults, but underestimated energy intake in obese adults [24].

Although older adults are often included in validation studies, they are not the primary focus [20], and few studies have focused primarily on older hospitalized adults. Boullata et al. [22] evaluated the accuracy of these equations in a population of hospitalized patients, where approximately one-third of the sample was aged 68 through 92 years. The authors determined that none of the predicted equations accurately estimated REE in hospitalized patients. Although the Harris-Benedict, with an applied factor of 1.1, had the highest percentage of accurate predictions compared to the other equations, nearly 40% of patients' energy expenditures were predicted inaccurately. The authors extrapolated that this error could equate to an over- or under-estimation of energy expenditure by nearly 400 kcals [22]. Kross et al. [25] examined mechanically ventilated patients in the intensive care unit with a mean age of 49.9 (SD ± 17.6) years, and although the Harris-Benedict equation was the most precise, the predicted value was within 10% of the measured value in only 31% of patients. Further, Neelemaat and colleagues [42] examined a population of malnourished (BMI < 20 and/or recent significant weight loss >5% in 1 month or >10% in 6 months) adults ≥60 years and compared 23 predictive equations to indirect calorimetry upon hospital admission. Findings suggest the best prediction equations accurately predicted energy expenditure in only 40% of patients. The range of under-prediction across predictive equations described by Neelemaat and colleagues was 35–93%, while the range of over-prediction was 2–25%. This is alarming, considering Compher and colleagues [43••] reported that actual energy intake in their sample of patients from 202 intensive care units averaged between 60 and 70% of the recommended goal intake. This is similar to other studies examining permissive underfeeding that have reported intakes of the usual care or control group as ~60–70% of goal intake [29•, 44]. Collectively, these findings suggest that the rate of underfeeding and inaccurate predictions may not adequately address energy needs in the hospital setting among older adults.

In response to weak correlations as described, Savard et al. [19] validated a newly developed equation which used four variables (height, weight, temperature, and minute ventilation) against indirect calorimetry and compared this equation to other established equations suitable for mechanically ventilated patients. This equation demonstrated better accuracy in comparison to other equations; in Savard et al.'s equation,

Table 1 Summary of published predictive equations and accuracy compared to indirect calorimetry in older adults

Method	Equation[a]	Resting energy expenditure[b]
American College of Chest Physicians [10]	EE (ACCP) = 25 kcal × BW	↑ [20] ↓↓↓ [21] ↓↓↓↓ [22]
Bernstein [23]	Men: EE (Bernstein) = 11.02 × BW + 10.23 × height (cm) − 5.8 × age − 1032 women: EE (Bernstein) = 7.48 × BW + 0.42 × height (cm) − 3 × age + 844	↓ [24] ↓↓↓ [7, 25]
Faisy [19]	EE (Faisy) = 8 × BW + 14 × height (cm) + 32 × MV + 94 × TEMP − 4834	↑ [18]
Fredrix [26]	EE (Fredrix) = 1641 + 10.7 × BW − 9 × age − 203 × sex	↔ [24] ↓ [25]
Fusco [27]	EE (Fusco) = −983 − 4 × age + 32 × height (in.) + 11 × BW	↓ [18]
Harris-Benedict [28]	Men: EE (HB) = (66.5 + 13.75 × BW + 5.003 × height (cm) − 6.775 × age) × SF women: EE (HB) = (655.1 + 9.563 × BW + 1.85 × height (cm) − 4.676 × age) × SF	↔ [21, 24] ↓ [7, 20, 22, 25] ↓↓ [18, 29•]
Henry [30]	Men: 60–70 years: EE (Henry) = 13 × BW + 567 women: 60–70 years: EE (Henry) = 10.2 × BW + 572 men >70y: EE (Henry) = 13.7 × BW + 481 women >70y: EE (Henry) = 10 × BW + 577	↔ [24] ↓↓ [7, 25]
Ireton-Jones equation for obese individuals [31]	Men: EE (IJ) = 606 + (9 × BW) − (12 × age) + 400 (if ventilated) + 1400 women: EE (IJ) = BW − (12 × age) + 400 (if ventilated) + 1444	↑↑ [18, 20] ↓↓ [22]
Korth [32]	EE (Korth) = 41.5 × BW + 35.0 × height (cm) + 1107.4 × sex − 19.1 × age − 1731.2	↔ [24] ↓ [7, 25]
Lazzer [33]	Weight: EE (Lazzer) = (BW × 0.048 + height (m) × 4.655 − age × 0.020–3.605) MJ/d body composition: EE (Lazzer) = (FFM × 0.081 + FM × 0.049 − age × 0.019–2.194) MJ/d	↓ [25]
Luhrmann [34]	EE (Luhrmann) = (3169 + 50.0 × BW − 15.3 × age + 746 × sex) kJ/day	↔ [24] ↓ [25]
Mifflin-St. Jeor [35]	Men: EE (MSJ) = (9.99 × BW + 6.25 × height (cm) − 4.92 × age + 166) × SF women: EE (MSJ) = (9.99 × BW + 6.25 × height (cm) − 4.92 × age − 161) × SF	↔ [21] ↓↓ [7, 20, 24, 25] ↓↓↓↓ [22]
Muller [36]	EE (Muller) = 0.047 × BW − 0.01452 × age + 1.009 × sex	↔ [24] ↓ [25] ↓↓ [7]
Owen [37, 38]	Men: EE (Owen) = 879 + 10.2 × BW women: EE (Owen) = 795 + 7.2 × BW	↔ [24] ↓ [25] ↓↓↓↓ [22]
Penn State equation, standard [39]	EE (Penn State, standard) = 0.85 × HB + VE × 33 + Tmax × 175–6433	↓ [20] ↓↓↓↓ [21]
Penn State equation, modified [39]	EE (Penn State, modified) = 0.96 × MSJ + 31 × VE + 167 × Tmax − 6212	↓↓↓↓ [21]
Schofield [40]	Weight only: men > 60: EE (Schofield) = 0.049 × BW + 2.459/4.184 × 1000 women > 60: EE (Schofield) = 0.038 × BW + 2.755/4.184 × 1000 weight and height (m): men > 60: EE (Schofield) = 0.038 × BW + 4.068 × height − 3.491/4.184 × 1000 women > 60: EE (Schofield) = 0.033 × BW + 1.917 × height + 0.074/4.184 × 1000	↔ [24] ↓ [7] ↓↓ [25]
Swinamer [17]	EE (Swinamer) = −4349 + 945 × BSA − 6.4 × age + 108 × TEMP + 24.2 × RR + 81.7 × TV	↓ [20] ↑↑↑↑ [18]
WHO/AO/UNU [41]	Weight only: men > 60: EE (WHO) = 13.5 × BW + 487 women > 60: EE (WHO) = 10.5 × BW + 596 weight and height (m): men > 60: EE (WHO) = 8.8 × BW + 1128 × height − 1071 women > 60: EE (WHO) = 9.2 × BW + 637 × height − 302	↑ [24] ↓ [7, 25]

↑ Equation overestimates mean measured REE by 50 < 200 kcals, ↑↑ equation overestimates mean measured REE by 200 ≤ 350 kcals, ↑↑↑ equation overestimates mean measured REE by 350 ≤ 500 kcals, ↑↑↑↑ equation overestimates mean measured REE by >500 kcals

↓ Equation underestimates mean measured REE by 50 < 200 kcals, ↓↓ equation underestimates mean measured REE by 200 ≤ 350 kcals, ↓↓↓ equation underestimates mean measured REE by 350 < 500 kcals, ↓↓↓↓ equation underestimates mean measured REE by >500 kcals

ACCP American College of Chest Physicians, *BW* body weight (kg), *EE* energy expenditure, *FFM* fat free mass (kg), *FM* fat mass (kg), *HB* Harris Benedict, *RR* respiratory rate (breaths per minute), sex, *female* = 0, *male* = 1, *SF* stress factor, TEMP temperature (°C), *T Max* maximum body temperature in 24 h (°C), *MSJ* Mifflin St Jeor, *MV* minute ventilation recorded from ventilator in liters per minute, *REE* resting energy expenditure, *TV* tidal volume (L), *WHO/FAO/UNU* World Health Organization/Food and Agricultural Organization/United Nations University

[a] All equations provide kcal/day unless specified

[b] ↔ estimates ±50 kcals of mean measured REE;

weight was a less influential determinant than the Harris-Benedict equation. This distinction is important, given fluctuations that occur in weight during intensive care unit admissions. Savard's equation was also well-correlated with energy expenditure in subsets of patients with renal failure, infection, and those requiring inotropic and/or vasopressor support. However, the ability to draw conclusions from patients with multiple traumas, surgical conditions, or burns was limited [19].

In addition to these validation studies, the examination of racial differences in measured and predicted energy expenditure among older adults has been largely ignored [45]. After adjusting for fat-free mass among a sample of healthy older adults ($N = 288$), measured resting metabolic rate was lower in blacks than whites, suggesting there were racial differences in metabolic rate [46]. Compher and colleagues [45] examined the impact of Harris-Benedict and discovered that it significantly under-estimated energy requirements in older, hospitalized, African American patients; only 26% of patients had a measured energy expenditure value within 10% of the predicted value. Additional studies are needed to determine racial differences in energy expenditure, specifically among older adults.

Age-Related Conditions that Affect REE

Older adults have lower total energy expenditure and a lower physical activity level than younger adults [47, 48]. Fat-free mass is a large contributor to metabolic rate, and muscle mass is reduced with older age, most likely attributed to a decrease in physical activity. Risk of age-related sarcopenia [49], defined as a loss of muscle mass and low muscle strength or low physical performance, also increases with age [50]. Body mass index (BMI) is commonly used as an indicator of body fatness and is a less appropriate measure in older adults because of age-related changes in body composition and muscle mass decline [49]. Although fat-free mass is a large contributor to REE, studies suggest that there is also an age-associated reduction in basal metabolic rate that cannot be fully explained by a decrease in fat-free mass [51, 52].

Additionally, validation studies often exclude medication use and other conditions, such as hypertension, diabetes, and thyroid disease, which are known to affect the metabolic state. Thus, these equations may not be applicable to hospitalized patients. Agitation or restlessness may increase REE [17], whereas medications that induce sedation or analgesia, including but not limited to narcotics and benzodiazepines, reduce REE. A systematic review conducted by Dickerson and colleagues reported the reduction in metabolic rate ranged in the studies from 262 up to 680 kcals/day [53]. This review also reported that autonomic agents which induce skeletal muscle paralysis decreased REE on average by 11 to 33%, and cardiovascular agents such as beta-adrenergic receptor antagonists decreased REE by 4 to 12% [53].

It has been estimated that more than 75% of older adults have multiple chronic conditions (MCC) [5]. MCCs are defined as one or more conditions that "lasted or was expected to last twelve or more months and resulted in functional limitations and/or the need for ongoing medical care" [54]; examples of MCCs include but are not limited to asthma, diabetes, heart disease, hypertension, and chronic respiratory conditions. As the majority of the predictive equations were developed in a healthy population, MCCs that could affect metabolic rate are not considered in these predictive equations, resulting in inherent inaccuracies in calculating REE. In addition, it has been estimated that approximately 50% of hospitalized adults are prescribed greater than five medications [55]. This incidence of polypharmacy may also affect REE. Hospitalized older adults, particularly those admitted to the critical care units, often have one or more of these conditions and/or are currently using related medications. Widely accepted equations were not developed with these considerations, thus, necessitating the examination of predictive equation accuracy. Given that approximately half of patients admitted to the ICU are greater than 65 years of age and the majority of older adults have MCCs [4, 5], these patients are at an increased risk of mortality and functional limitations.

Obesity, Aging, and Critical Illness

The population of older adults in the USA continues to grow, as does the rate of obesity within this group. Adults over the age of 60 years are more likely to be obese than younger adults, and greater than 30% of older adults are obese [56]. Although controversial, data suggests that mild to moderate obesity (BMI 25–35 kg/m^2) may offer a survival advantage in obese patients compared to normal weight or underweight individuals (BMI <25 kg/m^2). This term, coined the "obesity paradox," is well-documented in patients with chronic illness including heart failure [57, 58], coronary artery disease [59], stroke [60], and COPD [61]. Mild to moderate obesity may also confer potential benefit among critically ill patients [62–66]. It is posited that obese patients have higher metabolic reserves, including more lean muscle mass, which allow them to survive [57]. For example, obese trauma patients are more likely to utilize muscle as fuel during critical illness than their non-obese counterparts [67]. Although mild to moderate obesity may have a protective effect on mortality, active life expectancy (i.e., the amount of remaining life a person can expect to live without disability) is diminished in obese older adults. Nonobese men and women can expect to live more active years, and fewer disabled years, than obese men and women [68]. Furthermore, a higher BMI among older adults has been associated with decreased physical functioning and vitality, which often negatively impact quality of life and the ability to perform basic personal care [69]. Obesity-related disability further decreases quality of life and places more burden on family members [68]. In one study, obesity was associated with significantly longer duration of mechanical ventilation and intensive care unit length of stay in critically ill patients [66]. This is important, given the associations with hospitalizations and functional decline in older adults, and suggests obesity status may lead to worsened conditions and quality of life following hospital discharge.

The amount of energy to provide to critically ill obese patients is a debatable topic: there is some debate whether permissive underfeeding may be beneficial [70]. Excess caloric intake may result in complications such as hyperglycemia, hepatic steatosis, and excess carbon dioxide production, which can exacerbate respiratory insufficiency or prolong weaning from mechanical ventilation [71]. This is further complicated by the inaccuracy of predictive equations when estimating energy needs in obese adults [24, 72]. Although Kross et al. [25] validated predictive equations in critically ill mechanically ventilated patients, they also determined accuracy in overweight and obese patients. Notably, among overweight patients, the Harris-Benedict equation under-estimated energy needs by 186 kcals/day. Among obese subgroups, the Harris-Benedict equation under-estimated between 203 and 277 kcals/day (depending on obesity class); the American College of Chest Physician's equation was the least precise [25]. Boullata et al. [22] found that there was a higher accuracy with actual body weight compared to adjusted body weight when using the Harris Benedict equation in obese patients.

Hypocaloric, high protein intake may be beneficial in the obese patient [10, 73], and the SCCM and ASPEN guidelines recommend using the weight-based equation of 11–14 kcal/kg actual body weight for patients with a BMI between 30 and 50, and 22–25 kcal/kg ideal body weight for those patients with a BMI >50. These simplistic formulas represent 65–70% of measured energy expenditure, providing a suggested estimate when indirect calorimetry is unavailable in the clinical setting [10].

Other Methods of Assessment in Hospitalized Patients

None of the current predictive equations accurately estimate reference energy expenditure values; thus, alternate approaches are sought to more closely estimate adequate energy intake. Rousing 2016 [21] compared seven predictive equations to measured REE in critically ill older patients, and found all predictive equations over- or under-estimated the reference energy expenditure value. The authors also compared a novel VCO_2-based calorimetry to indirect calorimetry and found that this method estimated energy expenditure accurately in 89% of patients. However, the author's approach may not be feasible in every setting, as there is a need for capnometer and software to analyze the VCO_2 values.

Hand-held calorimeters are another option to traditional indirect calorimetry methods. A review by Hipskind and colleagues [74] examined the validity and reliability of handheld or portable calorimeters in comparison to indirect calorimeters in hospitalized patients. The mean caloric difference between handheld devices and traditional metabolic cart was less than 200 kcals/day. Furthermore, the handheld calorimeters were more accurate than predictive equations. These devices may provide a welcome alternative to high cost indirect calorimetry methods and/or less accurate predictive equations when measuring REE.

Outcomes and Conclusions

Collectively, there remains a void in the literature with regard to attaining a balance of maximizing energy and nutrient delivery without overfeeding older hospitalized adults, in order to maintain adequate protein and calories for healing and maintaining muscle mass. Older adults have much higher rates of health care utilization than younger adults, and patients admitted to the ICU often experience a collection of health problems including muscle weakness/atrophy and cognitive dysfunction as a result of the ICU stay. Older adults have a greater prevalence of hospitalizations including critical care admissions, longer length of stay, and increased costs relative to younger adults [75–78]. Given that the growth within this population is expected to double by 2060, assessing strategies to reduce health care utilization, particularly related to intensive care utilization, is important.

Malnutrition is associated with complications that can lead to longer length of hospital stays, and increased morbidity and/or mortality rates. Although malnutrition is prevalent in the health care setting, it is commonly associated with significant recent weight loss or underweight classification, thus, is often overlooked by the practitioner in the obese patient. Estimates suggest only half of malnourished patients are recognized and treated [9], complicating recognition for revised energy needs among these patients. Neelemaat et al. [42] determined that most predictive equations under-estimate energy needs among malnourished patients, and few studies have adjusted for malnutrition or examined the prevalence of malnutrition in obese hospitalized patients. Robinson et al. [79] found that obese patients with malnutrition had higher mortality rates at 90 days than those without malnutrition (30.4 vs. 18.9%, respectively). Hence, it is imperative that nutritional status and targeted nutrition therapy remain a primary focus among all hospitalized older adults. Further, obesity should not be used as a factor in a practitioner's decision to withhold feedings or limit nutritional intake [10]. For all patients, energy needs should be assessed frequently during hospitalization.

In alignment with the 2016 ASPEN and SCCM guidelines, nutritional status should be assessed in all patients admitted to the hospital [10]. A number of screening and assessment tools to determine nutrition status exist, such as the Malnutrition Universal Screening Tool, Nutritional Risk Screening 2002 (NRS 2002), Mini Nutritional Assessment, Short Nutritional Assessment Questionnaire, Malnutrition Screening Tool, and the Subjective Global Assessment [80]. The ASPEN and SCCM guidelines state that only the NRS 2002 and the recently developed NUTRIC score [81] determine both nutrition status and disease severity and have been validated in the critically ill population [10]. There is limited data available on the prevalence and/or assessment of malnutrition in critically ill obese patients [79], and given that assessment of nutritional status is difficult in the critical care setting [10], additional research is needed to refine the current tools or develop new methods to assess nutritional status in this population.

While there are negative clinical outcomes associated with both under- or over-feeding [11–16], controversy regarding the optimal nutritional intake of critically ill patients exists. Some studies have demonstrated negative outcomes when achieving goal energy needs, and support reducing overall energy targets [82–84], while others have reported favorable outcomes with energy intake within recommended goals [85–88]. This may also be mediated by baseline nutritional risk status [43••, 86]. The importance of adequate and optimal levels of protein intake during hospitalization is also being explored, and may influence clinical outcomes [43••, 89, 90]. *Although beyond the scope of this review, the estimation of protein requirements in hospitalized older patients has been examined by others [91–93] and certainly warrants further attention*. An additional concern is the frequency for which enteral nutrition is held in the ICU, therefore, reducing the number of patients who will consistently meet their nutritional intake goals. Enteral nutrition is held for a number of reasons in the critically ill patient, which include but are not limited to tests and procedures that require the patient to leave the floor, prolonged preparation for extubation, and/or gastrointestinal complications and feeding intolerance, exhibited by high levels of gastric residuals, vomiting, and/or aspiration risk. This may be particularly relevant when considering the rate of under-prediction when utilizing predictive equations; without an accurate representation of true energy needs, it is difficult to ascertain the benefits or harms of meeting prescribed nutritional goals. *Using the results from this narrative review, the authors' recommend using indirect calorimetry as the primary determination for calculating energy needs if the measurement is available and if conditions (i.e., respiratory instability) that will affect the accuracy of the measurement are not present [22]. There are a number of published predictive equations, but no single equation consistently outperforms others in hospitalized older adult populations, while considering anthropometric values, race, and comorbidity status [22]. In many studies, the Harris-Benedict equation had the highest sensitivity compared to other equations, but inaccuracy ranged from 40 to 70%, depending on the population of interest. Given the inaccuracy of predictive equations that are frequently used to calculate energy needs in these studies, more clinical trials are needed to determine the most optimal nutritional intake in the older, hospitalized population.*

As the body of research demonstrating the importance of nutritional supplementation in older, hospitalized patients grows, more accurate equations which account for MCCs, polypharmacy, reduced muscle mass, and advanced age are needed to predict nutritional requirements. The development and validation of such an equation will be an initial step in precipitating a culture shift which places a greater emphasis on the importance of nutritional delivery as a therapeutic intervention, rather than supportive care.

Compliance with Ethical Standards

Conflict of Interest Elizabeth A. Parker, Termeh M. Feinberg, Stephanie Wappel, and Avelino C. Verceles declare they have no conflict of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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