

## REVIEW

## Measuring energy expenditure in clinical populations: rewards and challenges

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The measurement of energy expenditure (EE) is recommended as an important component of comprehensive clinical nutrition assessments in patients with altered metabolic states, who failed to respond to nutrition support and with critical illness that require individualized nutrition support. There is evidence that EE is variable in patients with metabolic diseases, such as chronic renal disease, cirrhosis, HIV, cancer cachexia, cystic fibrosis and patients under intensive care. By using appropriate techniques and interpretations of basal or resting EE, clinicians can facilitate the adequate nutrition support with minimum negative impacts from under- or overfeeding in these patients. This review is based on our current understanding of the different components of EE and the techniques to measure them, and to re-examine advances and challenges to determine energy needs in clinical populations with more focuses on the obese, pediatric and elderly patients. In addition, technological advances have expanded the choices of market-available equipments for assessing EE, which also bring specific challenges and rewards in selecting the right equipment with specific performance criteria. Lastly, analytical considerations of interpreting the results of EE in the context of changing body composition are presented and discussed.

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## INTRODUCTION

Establishing a patient's energy expenditure (EE) is an important step in determining nutritional needs. EE has three main components: basal metabolic rate, thermic effect of food or diet-induced thermogenesis, and physical activity EE. Many factors, such as age, body composition, thyroid hormones, catecholamines, ambient and body temperature, disease states and drugs/treatments influence these components to some extent and thus total EE. Basal metabolic rate (BMR), the minimal amount of energy expended for homeostatic processes, is a major component (about 60–80%) of total EE in free-living individuals and is an even larger component for hospital-bound patients due to a decreased level of physical activity. It is worth noting that resting EE is oftentimes used interchangeably with BMR in the literature and in clinical practices; however, in a strict sense, BMR is the lowest level of EE and could be up to 10% lower than resting EE (or sometimes called resting metabolic rate, or RMR), as BMR should be performed in conditions such as complete resting posture, post 8-h sleep (typically performed after an overnight in-patient stay), post 12-h fast, in a thermal neutral room temperature setting, and with darkened or dimmed lighting and quiet ambient conditions. In contrast, resting EE measurements can have fewer restrictions.

Fat-free mass has been found to be the strongest determinant of between-individual variability of BMR during weight-stable periods and after moderate weight loss.<sup>1–4</sup> Thermic effect of food represents the increase in EE above resting EE (around 8–12% of the energy intake) following meal ingestion and has been linked

to nutrient composition and energy content of food consumed. The last component of EE, physical activity EE, is defined as the additional EE (above resting EE) needed to perform physical activities, which can be further divided into exercise and non-exercise activity thermogenesis. Physical activity EE varies widely within and across individuals. For most sedentary individuals, and hospitalized patients purposeful exercise is minimal, whereas for those who participate in regular physical activity, exercise EE is generally 15–30% of the total daily EE.<sup>3,5,6</sup>

Any state of disease, whether critical or not, may directly or indirectly alter components of EE and subsequently have marked effects on nutritional status.<sup>7</sup> An accurate assessment of EE is necessary to determine caloric needs and to provide optimal nutrition support for in-patients, as well as nutrition counseling for outpatients. EE and nutritional needs in critically ill patients have been studied extensively owing to the impact of nutritional deficits on clinical outcomes. The benefits of optimal nutrition for the treatment of the severely ill and for the management of the chronically ill are well-documented.<sup>8</sup> Given the ever-evolving influence of societal factors on body weight and EE, re-examining advances and challenges to determine energy needs in clinical populations is essential. In addition, technological advances have yielded more widely available equipment that is relatively easy to operate for measuring EE, which warrants evaluations in a variety of populations as well as comparisons to accepted standards. Therefore, practical and analytical challenges of obtaining good measurements and interpreting the results of EE are being presented and discussed.

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## MATERIALS AND METHODS

EE ultimately refers to the net amount of energy the animal utilizes to maintain its biological functions, described by Kinney *et al.*<sup>9</sup> as 'central to life'. Researchers have been interested in understanding the energetic budgeting and regulation for more than a century. However, its relevance in clinical application has not always been appreciated. The initial surge of measuring BMR in hospitals and clinics for evaluating thyroid dysfunction in the 1920–1940s gradually yielded to chemical assessments of iodine metabolism in 1950s. The practice regained some momentum in 1970s as the result of interests for obesity research, sports medicine, rapid growth in individual-based clinical care and nutritional support for hospital patients.<sup>9</sup> However, the technology was a major challenge for practitioners before the 1980s. In the past 25 years, automated and user-friendly systems have been developed and established as routine measurements in clinical research and care facilities worldwide.

### Measurement of EE

The study of EE relies on calorimetry, either by measuring heat loss from the patient directly (direct calorimetry) or by measuring gas exchanges during respiration (indirect calorimetry). Direct calorimetry focuses on thermoregulatory biology and is conducted accurately in well-controlled environmental chambers. However, the clinical and practical application using this technique is quite limited. In contrast, indirect calorimetry techniques are commonly deployed for quantifying human EE in research and clinical applications both in controlled and field settings. The detailed measurement principles and application considerations have been published previously.<sup>10,11</sup>

As most clinical applications use indirect calorimetry to assess EE, we will briefly overview this method and point out the subtle differences in some systems that could lead to potential errors in measurement. It has been recognized for over a century that metabolic conversion of food energy has a varying heat of combustion or releases a different amount of energy per unit of oxygen used (oxidation), depending on which substrate/fuel is being converted (carbohydrate, protein or fat). Thus, by measuring oxygen consumption ( $\text{VO}_2$ ) and carbon dioxide excretion ( $\text{VCO}_2$ ), the net energy released from the fuels is being expended, which is typically expressed as calories (or kilocalories, kcal or KJ) per unit of time (min to 24 h) by using standard equations, such as the commonly used Weir's equation:<sup>12</sup>

$$\text{EE}(\text{kcal}) = 3.941 \times \text{VO}_2(\text{L}) + 1.106 \times \text{VCO}_2(\text{L}).$$

There is a small contribution by protein oxidation as measured by nitrogen excretion in the urine, which can be neglected without much added error unless the patient's protein turnover is substantially high (estimated 1% error in each 12% total calorie from protein oxidation).<sup>7</sup>

Using this principle, most clinical measurements of BMR or resting EE are performed using indirect calorimetry systems. In fact, the nomenclature 'indirect calorimetry' has been used interchangeably with BMR and resting EE by some practitioners and manufacturers.<sup>13</sup> There are several different types of metabolic carts with simultaneous  $\text{VO}_2$  and  $\text{VCO}_2$  measurements for both resting EE and physical activity EE (most common in clinical measurement settings). Other methods include portable systems that measure resting EE by  $\text{VO}_2$  only, wearable systems that measure physical activity EE by  $\text{VO}_2$  and  $\text{VCO}_2$ , whole-room calorimeters that measure dynamic EE continuously over 24 h or longer by  $\text{VO}_2$  and  $\text{VCO}_2$ , and doubly labeled water that measures average daily free-living EE by  $\text{VCO}_2$ . The last two methods are mostly applicable in research as they are technically challenging and costly,<sup>10</sup> and thus will not be discussed in this review.

Metabolic carts (shown in Figure 1) are the current standardized equipment for determining resting EE in clinical and field settings. This method consists of a gas collection/sampling system (face-mask, mouthpiece or a domed hood/canopy), a ventilation/flow rate-sensing system, oxygen and carbon dioxide gas analyzers, one or more calibration gas bottles (mixed gases with verified concentrations for  $\text{O}_2$ ,  $\text{CO}_2$  and typically balanced with  $\text{N}_2$ ), environmental assessments (temperature, humidity and barometric pressure) and a central computer to interface among all the measurement components and with the user. Currently, there are three different types of  $\text{O}_2$  analyzers commonly used in metabolic cart systems, paramagnetic, electrochemical (fuel cell), and zirconium oxide, while most  $\text{CO}_2$  analyzers still rely on the non-dispersive infrared sensors.<sup>11</sup> Despite the technical differences, properly maintained and calibrations should yield comparable performances between metabolic carts. In practice, however, different methods of sampling gases and measuring ventilation rates could lead to variability in resting EE results. For example, face-masks or mouthpieces may cause discomfort and anxiety in some patients,<sup>14</sup> and



**Figure 1.** Resting EE measured by an indirect metabolic cart system at the NIH Clinical Center.

thus may increase respiratory effort and/or decrease compliance of resting quietly over the duration of the assessment period. The canopy system may induce claustrophobia and the 'white' noise may cause the subject to fall asleep. In fact, these factors are likely to contribute more errors and variability into the end measurement outcome than the analyzers themselves.

To improve indirect calorimeter measurements, Wooley *et al.*<sup>15</sup> recommended a series of steps to standardize the environmental conditions, including preparing the patients and the care staff, as well as minimizing food, medication and other procedural influences (such as feeding and/or breathing tubes, blood pressure and blood draws, and so on). These recommendations should be built into the standard operating procedures of resting EE measurement practices.

**Accuracy, validity, reliability and sensitivity of indirect calorimetry.** There are several published studies evaluating the performance of metabolic carts, which address the issues of accuracy, validity, reliability and sensitivity; however, the use of these terms are not always clear. In an excellent technical review, Macfarlane<sup>16</sup> focused on comparing how different metabolic cart systems are used for exercise testing. Much of the technical details are also pertinent to the resting metabolic cart measurements.

Accuracy is defined as the closeness of the measurement to a true value, and refers to the specific measurement with a metabolic cart system. For example, the accuracy of the analyzers can be directly compared with a known traceable standard, such as reference gases with true concentration values. However, as the market-available calibration gases used for routine calibration of metabolic carts are not typically calibrated against highly traceable standards (such as from the National Institute of Standards and Technology-certified metrology labs), the accuracy of the analyzers after calibration are merely a relative measure within the lifespan of each calibration gas container(s). The true accuracy of a metabolic cart system is difficult to measure as it integrates the accuracies and balances the errors of all the sensors and operation factors.

Validation refers to how a measurement compares to another similar measure (with the assumption that latter has the acceptable accuracy), or to a standard procedure/input with measurable outcomes. For example, different metabolic carts have been 'validated' against the Douglas bag method,<sup>17</sup> an established metabolic cart system (for example, Deltatrac II; VIASYS Healthcare Inc., SensorMedics, Yorba Linda, CA, USA), and/or alcohol burns. The study by Cooper *et al.*<sup>18</sup> is a good example of such a validation study, where six metabolic cart systems were included. The Deltatrac II was used as the common reference criterion to which the remaining five systems were compared. The sample size of each within-subject comparison group was 10–17, and the between-instrument coefficient of variation in measured resting EE ranged from 5.4 to 12.2%. Only one was found to be statistically different from the reference Deltatrac II carts, but the 95% confidence intervals of the difference were as wide as around 600–1000 kcal.

Reliability is generally the ability of the system (or a measurement procedure) to perform at different times. It is commonly reported as repeatability within an individual or between alcohol combustion tests (coefficient of variation). It has been reported that systems such as the

Sensormedics 2900 (Yorba Linda, CA, USA) and the Deltatrac MD 1 (Datex, Helsinki, Finland) could achieve a coefficient of variation of 2% or less,<sup>19</sup> and the Deltatrac II resulted 3.0–3.6%.<sup>18</sup>

Sensitivity is the magnitude of change that is measurable by the system. Depending on the analyzer, calibration gases, ventilation rates sensors and the analytical processing (data smoothing), the sensitivity of metabolic carts can vary significantly. The term precision can sometimes be used to refer to sensitivity. Although there are some reports and recommendations related to sensitivity for metabolic carts in exercise tests ( $\dot{V}O_{2\max}$ ),<sup>16</sup> very limited data exist in the resting EE measurements. This is partly due to the lack of a calibration system that can provide a dynamic or graded input to the indirect calorimeter, which is similar to a phantom for an imaging system (for example, a magnetic resonance imaging scanner).

## CLINICAL APPLICATIONS

In clinical care settings, indirect calorimetry has been used in patients in whom altered EE is suspected or conventional nutritional support fails to respond. Previous reviews have addressed measuring resting EE in specific patient populations, such as chronic renal disease,<sup>20,21</sup> adult intensive care unit patients,<sup>14</sup> pediatric intensive care unit patients,<sup>22</sup> cystic fibrosis,<sup>23</sup> cancer cachexia,<sup>24</sup> HIV<sup>25</sup> and cirrhosis.<sup>26,27</sup> It also has been used serially (for example, at baseline and frequent follow-ups) timed with changes in nutrition support of critically ill patients as a marker of their response to stress.<sup>14,15</sup> In these patients, resting EE measurements are designed to optimize nutrition care and facilitate the prevention of complications related to under- or overfeeding. In other populations, however, EE measurements are also important, as described below.

### Obese population

As a result of the obesity prevalence increasing more than twofold in the past 30 years,<sup>28</sup> the critically ill obese patient is becoming more prevalent. EE in obese patients is highly variable, making it challenging to determine accurately energy needs. Recent analyses indicate that predictive equations estimated resting EE within 10% of measured rate in only 38–70% of non-hospitalized obese patients<sup>29</sup> and even in fewer patients when assessing hospitalized obese patients.<sup>30,31</sup> In general, predictive equations tend to overestimate the energy requirements in obese patients, while the Mifflin–St Jeor equation has been found to yield the closest prediction compared with measured resting EE.<sup>29,31,32</sup> Owing to an increasingly sedentary lifestyle as well as the vast availability of energy-dense foods, the patients of today, both inpatient and outpatient, are very different than those studied decades ago. Predictive equations include only weight as a variable and these analyses illustrate the limitations associated with using predictive equations in samples dissimilar to those from which they were derived. A consensus regarding which weight to use (that is, actual weight, ideal weight, adjusted weight, and so on) is lacking in the literature.<sup>33</sup> Given the difficulty in accurately determining energy needs for obese patients, using indirect calorimetry is advised to get an individual estimate of nutritional needs.

Although some studies indicate that obese patients who are critically ill are at an increased risk of complications and poor outcomes,<sup>32,34</sup> others indicate that excess body weight might actually be protective, possibly due to greater energy stores.<sup>35,36</sup> Thus, even when using indirect calorimetry to determine EE, the debate about best-practice nutrition support continues in regards to whether or not permissive underfeeding should be used in these patients. Proponents of hypocaloric feeding argue that obese patients can use 'sufficient amount of adipocyte fat stores for fuel, while opponents argue that these patients may not be able to mobilize fat for oxidation.<sup>37</sup> The optimal nutrition recommendation for critically ill obese patients remains unclear.

On the other hand, measuring EE may be useful in obese subjects who seek weight loss interventions. Due to the complicating nature of changes in body weight (or in body composition) and the noted inaccuracies of prediction equations before, during and after weight loss, indirect calorimetry can be beneficial in the clinical practice of weight management if used carefully and appropriately. Correctly determining the energy needs in this population is essential as dietary changes are the primary predictor of weight loss.<sup>38</sup> Being able to provide patient-specific recommendations may enhance the possibility of weight loss success, as well as weight maintenance, if EE is continually reassessed as body weight changes. Furthermore, research indicates that patients are more successful when following an individualized behavioral intervention. Collectively, these data support recommendations for using indirect calorimetry to obtain the most accurate assessment of calorie needs for hospital-bound patients who are prone to energy imbalance, and for obese patients and formerly obese patients in both the in-patient<sup>39</sup> and outpatient settings.

Practical challenges in measuring resting EE or BMR in obese population include the higher chance of breathing irregularities, either as a result of the patient's sleep apnea and/or the supine position recommended for BMR may not comfortable for the patient. These factors can cause patients to fall asleep during the measurement, discomfort and/or cause inconsistent ventilation patterns, which ultimately lead to more errors or noise in the EE measurements.

### Elderly population

The unique medical and nutritional needs of the elderly indicate that, these individuals are another group requiring special considerations when EE is measured to aid in determining energy requirements. Currently, one out of nine people are over the age of 60 years; and by 2050 it is estimated that 20% of the world's population will be aged 60 years or more.<sup>40</sup> Furthermore, the population group 80 years or older is the fastest growing segment of the older population. The growing aging population is anticipated to lead to an increase in the number of people at high risk of disability and morbidity, both of which can be influenced by energy intake and perhaps by EE. There is limited data regarding energy requirements of the elderly. Given the diversity of this group—some are institutionalized, sick, frail, using multiple medications or homebound, while others are free-living and healthy—population estimates are difficult to obtain.

However, at the present time, it is well-documented that the impacts of aging on body composition greatly influence the nutritional needs of an individual. With aging, adipose tissue increases while lean mass decreases. Resting EE decreases approximately 2–4% with each decade,<sup>41,42</sup> mostly due to the changes in body composition changes. In addition, the elderly tend to be less physically active, which also leads to lower total EE. Thus, the prevalence of overweight and obesity is increasing in this segment of the population.<sup>28</sup> However, the issues of underweight and malnutrition still are pertinent to this population group as well. Illness severity is associated with increased energy and protein requirements, and inadequate nutrition is linked with poorer outcomes in the critically ill. Yet, as mentioned earlier, there is an ongoing debate regarding permissive underfeeding in the obese critically ill patient. Therefore, weight management with this group is very challenging and complex in part due to comorbidities that are not present in younger adults. In general, weight loss is associated with a decrease in both fat mass and lean body mass; the latter effect is more undesirable in the elderly as it can worsen the underlying age-related sarcopenia and decrease in bone mineral density. Furthermore, changes in EE in the elderly may contribute to signs of frailty, such as weakness, inactivity, fatigue and reduce

food intake—all of which may lead to unintentional weight loss and/or be signs of more serious underlying health problems, such as cancer. The accurate assessment of energy needs of the aging population is important for minimizing malnourishment, excess body weight and comorbidities. Although Gaillard *et al.*<sup>43</sup> carefully reviewed the literature surrounding the energy requirements of the elderly, few studies have determined the needs of population age over 80 year of age.<sup>44</sup> Furthermore, indirect calorimetry to assess resting EE in older adults is clinically indicated as predictive equations were not derived or validated in this population. Currently, the use of these equations is widespread; however, the importance of individualized nutrition, based on indirect calorimetry, will continue to grow as this segment of the population grows.

Similar to the obese population, the main practical challenge of measuring BMR and resting EE in this population is the patients' ability to remain restful and breathe smoothly throughout the measurement period (typically 20–30 min). In addition, the environmental temperature may need to be increased to satisfy the criterion of thermoneutrality as it has been shown that thermal preference is affected by age.<sup>45</sup>

#### Pediatric population

Measuring EE at the other end of age spectrum (that is, in children) is challenging for numerous reasons, most notably the ever-changing energy needs for growth and levels of physical activity. Energy demands for growth constitute approximately 40% of total EE during the first month of life, 6% by month 6, <2% during the second year of life and 1–2% during adolescence.<sup>46</sup> The EE of infants can be influenced by other factors, such as birth weight, whether they are breastfed or formula fed and disease state.<sup>46</sup> Studies indicate that low-birth-weight infants have higher total EE than healthy term infants,<sup>47,48</sup> and that spontaneously breathing low-birth-weight infants have higher total EE than ventilated low-birth-weight infants.<sup>49</sup> Feeding practices also influence the total EE of infants such that formula-fed infants have higher total EE during the first year of life than breastfed infants.<sup>50,51</sup> Another consideration for determining total EE during infancy and childhood is the level of habitual physical activity, which can yield interindividual coefficients of variability as high as 34%<sup>52–54</sup> and tends to decrease with age given environmental changes, which encourage sedentary behavior.<sup>55</sup> With the increasing prevalence of overweight and obesity among children and adolescence<sup>56,57</sup> and its impact on body composition, measuring EE and/or body composition may be of greater importance when assessing a child's nutritional needs.

However, currently there is no standard protocol for measuring resting EE in children and a variety of methods are used.<sup>7</sup> Owing to the necessary adherence to strict conditions, such as fasting and remaining at rest before and during measurement, indirect calorimetry can be challenging among children. Studies indicate that children become restless during the evaluation period and the use of shorter protocols has been suggested to decrease fidgeting and boredom.<sup>58,59</sup> Mellecker *et al.*<sup>60</sup> evaluated an abbreviated protocol and determined that it is valid among healthy children and may increase compliance. Despite these promising findings, the expense of the calorimeters, the time required for measurements and the need for trained personnel to run the tests hamper the wide use of indirect calorimetry outside of critical care units.<sup>61</sup> Thus, predictive equations are most commonly used to assess nutrition needs among pediatric inpatients and outpatients. For children, response to nutrition support and interventions is assessed by monitoring health status and identifying deviations from normality through the use of growth charts<sup>62–64</sup> and subsequent adjustment as needed.

Although the WHO has stated that there is an urgent need for additional studies assessing resting EE and total EE in elderly and

pediatric populations worldwide to develop equations that better predict nutritional needs throughout the life cycle and across a variety of races/ethnicities and stages of growth and development,<sup>46</sup> indirect calorimetry and the doubly labeled water method are not widely used in the clinical setting,<sup>65</sup> and portable and less burdensome methods is becoming increasingly more common.<sup>66,67</sup>

#### DISCUSSIONS

In patients whose metabolic status may be altered by diseases, medications, treatments and especially when confounded by obesity, and/or by age, measuring BMR or resting EE using indirect calorimetry (metabolic carts) may offer a major advantage over using predictive equations such that the closest nutrition support regimens could be 'matched' to the individual needs. However, it is also critical that we are aware of the challenges in performing these measurements in general and specific populations and optimize the measurements for clinical care.

It is not uncommon to categorize patients into normal, hypo- or hypermetabolic states by comparing measured resting EE with predicted 'norms'. The norms usually come from a set of predictive equations derived for determining BMR or resting EE (resting metabolic rate). Four prediction equations identified as the most commonly used in clinical practice for adults are Harris–Benedict,<sup>68</sup> Mifflin–St Jeor,<sup>69</sup> Owen<sup>70,71</sup> and World Health Organization/Food and Agriculture Organization/United Nations University (WHO/FAO/UNU)<sup>72</sup> equations. Each of these equations was derived from different patient populations and thus has different clinical applications and limitations. For example, Harris–Benedict was derived from data provided by healthy, normal-weight Caucasian adults between 1907 and 1917. In contrast, the Mifflin–St Jeor equation was derived from data collected in the 1990s from a population across a wide range of body weights (that is, normal through severely obese). Although predictive equations are easily accessible and do not require specialized equipment, significant error can occur when using them to determine the energy needs of an individual. Moreover, some of the equation may be 'out of date'. For example, Müller *et al.*,<sup>73</sup> showed that the WHO equation systematically overestimated resting EE at lower resting EE values, while underestimated at high resting EE values in a large and heterogeneous German population (a modern and affluent population segment).

The general convention is that predictive regression equations perform best for groups of people instead of individuals.<sup>29</sup> Furthermore, there are conflicting results in the literature as to which equation is best suited for a general patient population. For example, one analysis indicates that despite a clinically relevant error rate of 20%, the Mifflin–St Jeor equation has the most accuracy and lowest magnitude of error and should be used among healthy non-obese and obese adults,<sup>29</sup> while a more recent analysis indicates that the Harris–Benedict equation and two adaptations of the WHO/FAO/UNU equation outperform the Mifflin–St Jeor equation in this population.<sup>74</sup> The WHO/FAO/UNU and Schofield equations<sup>75</sup> adapted for children appear to be the best estimates of resting EE in children and adolescents.<sup>76–78</sup> However, an FAO/WHO/UNU Expert Committee cautions against using a single equation when estimating resting EE of boys and girls across all racial groups, which warrants new equations be derived for various races.<sup>79</sup>

Cautions should be taken in comparing measured resting EE to predictive values with simple normalized body weight, such as 15 or 20–25 kcal/kg body mass per day for overweight and obese adults,<sup>80</sup> or proposed by Kleiber.<sup>81,82</sup>

$$\text{RMR}(\text{kcal}/\text{day}) = 70 \times \text{bodymass}^{0.75}$$

While this negative allometric relationship exists across a wide range of mammalian species with variable body mass, it still does

not completely mitigate the mathematical artifact caused by the non-zero intercept that exists in the regression equation between EE and body mass in humans.<sup>83,84</sup>

Whenever possible, body composition should be measured using validated techniques, which yield fat and fat-free masses. While there are advantages and limitations with each technique, dual energy X-ray absorptiometry, whole-body densitometry, bioelectrical impedance analysis and computer tomography all measure body composition with good accuracy.<sup>85</sup> Clinicians and researchers can then apply the components of body masses into predictive equations for BMR or resting EE in non-diseased populations and/or to specific disease conditions.

Comparison of resting EE before and after a change in body weight is also challenging. With the strong relationship between body composition and resting EE, the potential changes in resting EE beyond what would be expected by the changes in fat and fat-free mass have been studied and debated.<sup>86,87</sup> A recent systematic review by Schawtz *et al.*<sup>4</sup> found that an average weight loss of 9.4 kg ( $\pm 5.5$  kg) did not result in a significantly greater change in resting EE after statistical corrections of the changes in fat and fat-free mass. This study further emphasized that one should use caution when adjusting resting EE measures with body composition. In a recent study of patients who had undergone Roux-en-Y gastric bypass surgery,<sup>88</sup> the dramatic change in total and sleeping EE (measured by a metabolic chamber) from baseline to 6 months postop was mainly explained by the reduction in fat-free mass and fat mass, and no additional metabolic adaptation was observed. However, the debate is far from settled in this question whether weight fluctuation, in particular, weight cycling changes resting EE beyond the changes in body composition. The physiological impacts of weight cycling have been shown to alter substrate utilization, which also affects the nutrient needs of this population.<sup>89,90</sup>

On the other hand, malnutrition in patients is commonly associated with the loss of lean muscle mass, poor wound healing, increased risk of infection, impaired immunity, organ dysfunction and increased morbidity and mortality.<sup>91</sup> Thus, monitoring a patient's physiologic and metabolic responses during illness is essential for optimal clinical care, and in particular nutrition support. Furthermore, under- and overfeeding can have deleterious effects on medical outcomes in the critically ill patient, so it is important to obtain a baseline assessment of the degree of metabolic response to injury followed by intermittent or continuously measures until a steady state is achieved.<sup>92</sup> Indirect calorimetry provides accurate assessments of energy needs as they change and subsequently appropriate nutrition support while a critically ill patient recovers.

Most indirect calorimetry systems (if equipped with a CO<sub>2</sub> analyzer) calculate the ratio of VCO<sub>2</sub> and VO<sub>2</sub>, and express it as respiratory quotient (RQ) or respiratory exchange rate. It is been used as an indirect index of substrate utilization, which in theory an RQ = 1.0 represents that all metabolism comes from carbohydrates and conversely an RQ = 0.7 indicates that all comes from fat, respectively. However, since humans are 'flex-fuel users' and mixed biological processes are simultaneously taking place (for example, fat oxidation and lipogenesis), a short-term RQ or respiratory exchange rate measure should not be overtranslated into guidelines to modify nutritional regimens. Moreover, it has been recommended that the RQ or respiratory exchange rate reading (within a range of 0.67–1.3) should only be used as an index of practical validity of the in resting EE assessment.<sup>15</sup>

Although indirect calorimetry is the recommended method for determining EE, this method is not without limitations. First, resources can be a barrier to indirect calorimetry as the equipment is expensive and trained personnel may be lacking.<sup>93</sup> There also are numerous technical aspects of measuring indirect calorimetry that need to be considered to increase the accuracy of measurements. From the physiological perspective, there are

multiple challenges to determining energy needs as well. During critical illness, energy needs may fluctuate and some medical conditions and disease states, such as cancer, differentially impact EE, making it difficult to determine accurately calorie needs. In addition, age, medications, stress factors and body composition can impact EE. Lastly, population-wide changes, such as the increasing prevalence of overweight and obesity, create new challenges in both in-patient and outpatient settings when determining energy needs.

## CONCLUSIONS

Compared with estimating EE using body weight, height, age, sex and even measured fat-free and fat masses, indirect calorimetry (that is, metabolic carts) provides more accurate energy requirements in a wide range of patients with altered metabolic states, different body sizes and age extremes. If the challenges of using this technology are properly considered and balanced, the valid resting EE measurements can be the minimum nutrition support targets to protect patients from under- or overfeeding.

## CONFLICT OF INTEREST

The authors declare no conflict of interest.

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