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Original article

# Predictive equations versus measured energy expenditure by indirect calorimetry: A retrospective validation

Oren Zusman [a, b, *], Ilya Kagan [b, c], Itai Bendavid [b, c], Miriam Theilla [c, d], Jonathan Cohen [b, c], Pierre Singer [b, c]

[a] Department of Cardiology, Rabin Medical Center, Beilinson Hospital, Petah Tikva, Israel
[b] Sackler School of Medicine, Tel Aviv University, Israel
[c] Department of General Intensive Care and Institute for Nutrition Research, Rabin Medical Center, Beilinson Hospital, Petah Tikva, Israel
[d] Nursing Department, Steyer School of Health Professions, Sackler School of Medicine, Tel Aviv University, Israel

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SUMMARY

*Background & aims:* Measuring resting energy expenditure (REE) via indirect calorimetry (IC) in intensive care unit (ICU) patient is the gold standard recommended by guidelines. However technical difficulties hinder its use and predictive equations are largely used instead. We sought to validate commonly used equations using a large cohort of patients.
*Methods:* Patients hospitalized from 2003 to 2015 in a 16-bed ICU at a university-affiliated, tertiary care hospital who had IC measurement to assess caloric targets were included. Data was drawn from a computerized system and included REE and other variables required by equations. Measurements were restricted to 5 REE per patient to avoid bias. Equation performance was assessed by comparing means, standard deviations, correlation, concordance and agreement, which was defined as a measurement within 85–115% of measured REE. A total of 8 equations were examined.
*Results:* A total of 3573 REE measurements in 1440 patients were included. Mean patient age was 58 years and 65% were male. A total of 562 (39%) patients had >2 REE measurements. Standard deviation of REE ranged from 430 to 570 kcal. The Faisy equation had the least mean difference (90 Kcal); Harris–Benedict had the highest correlation (52%) and agreement (50%) and Jolliet the highest concordance (62%). Agreement within 10% of caloric needs was met only in a third of patients.
*Conclusions:* Predictive equations have low performance when compared to REE in ICU patients. We therefore suggest that predictive equations cannot wholly replace indirect calorimetry for the accurate estimation of REE in this population.


## 1. Background

Measuring resting energy expenditure (REE) via indirect calorimetry (IC) is the gold standard recommended by guidelines [1], but technical issues hinder its use and the issue remains under debate [2]. For this reason, predictive equations are largely used in its place. These equations have been used for decades, starting with the Harris & Benedict prediction [3] followed by many others [4]. Despite the expectation that anthropometric measurements can predict energy expenditure, validation studies have shown wide-ranging and disappointing results [5–9]. A significant weakness of both the original studies deriving the equations and the validation studies relates to the fact that they were performed on dozens to several hundred patients at most, thus calling their generalizability into question. Since the estimation of caloric requirements guides daily clinical practice, accuracy in measurement is of paramount importance. However, with the exception of two [10,11], all clinical studies regarding caloric provision used predictive equations and not IC measured REE. It has been suggested that both overfeeding and underfeeding might be associated with mortality (a ‘U-shaped curve’) [12,13], so that a presumed ‘target’ as derived from potentially inaccurate equations could actually be detrimental. Indeed that optimal goal is still intensely debated. We have thus sought to validate several predictive equations compared with IC measurement made in our institution.

* Corresponding author. Department of Cardiology, Rabin Medical Center, Beilinson Hospital, Petah Tikva, Israel. Fax: +972 3 9376512.
*E-mail address:* orenzusman@gmail.com (O. Zusman).

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**Table 1**
Equations examined.

| Name | Equation |
|---|---|
| Faisy 2003 [4] | 8*(wt) + 14*(ht) + 42*(Ve) + 94*(T)-4834 |
| Fusco 1995 [36] | −983 − 4*(age) + 12.6*(ht) + 11*(wt) |
| Jolliet 1998 [19] | Males, age >60: 25*(wt)<br>Males, age <60: 30*(wt)<br>Females, age >60, 20*(wt)<br>Females, age <60, 25*(wt) |
| Harris Benedict 1918 [3] | Males: 13.75*(ht) + 5*(wt) − 6.8*(age) + 66<br>Females: 1.8*(ht) + 9.6*(wt) − 4.7*(age) + 655 |
| Ireton-Jones 1997 [17] | 1784 + 5*(wt) − 11*(age) + 244*(male) + 239*(trauma) + 804*(burns) |
| Mifflin-St. Jeor 1990 [18] | Males: 10*(wt) + 6.25*(ht) − 5*(age) + 5<br>Females: 10*(wt) + 6.25*(ht) − 5*(age) − 161 |
| Penn State 2003 [16] | 0.96*(MSJ) + 167*(Tmax) + 31*(Ve) − 6212 |

ht-height (cm), wt – weight (kg), Tmax – daily maximal temperature (C), Ve – minute ventilation (ml), MSJ – Mifflin St. Jeor.

## 2. Methods

We included all patients that were admitted to the Intensive Care Unit (ICU) of Rabin Medical Center, a 16-bed multidisciplinary unit in a university-affiliated tertiary-care medical center, from 2003 to 2015 and who underwent IC measurements (Deltatrac II, Datex-Ohmeda, GE, USA). This device is considered the most widely used and validated calorimeter. The calorimeter was calibrated for test gases (ambient air and $O_2$ 95% and $CO_2$ 5%) before all measurements and with ethanol on a monthly basis. Before testing, operators needed to ensure that patients were in a stable condition for at least half an hour, ventilated with $FiO_2$ less than 60% and PEEP less than 10 cm $H_2O$, without any discernable air leaks. Only measurements that were stable for at least 20 min were considered acceptable. Consumption of oxygen and $CO_2$ production were measured and calculation of the respiratory quotient (RQ) and REE were performed using the Weir equation [14]. The timing and number of IC measurement per patient were determined by the treating physician. We restricted the number of measurement to 5 per patient in order to both allow measurement at different times (and not only closest to admission) and to reduce bias from multiple single patient measurements. Tested predictive equations included 25 kcal/kg per day (ESPEN formula) [15], the Harris Benedict equation [3] without and with a stress/correction factor (of 1.3 that is usually used to accommodate critical illness), the Penn State University equation [16], the Ireton Jones equation [17], the Faisy equation [4], the Mifflin St -Jeor equation [18] and the Jolliet ESCIM equation [19]. We included all relevant measurements required by these equations as presented in Table 1. For each IC measurement, the equations were calculated according to the closest available measurement (e.g. temperature, minute ventilation). Equations are presented in Table 1. Agreement was defined as prediction within 85% and 115% of IC REE. Percent difference was defined as the absolute difference divided by measurements mean and percent error as the absolute difference divided by IC REE. Correlation is described as a Pearson's r as a ratio.

The study was approved by the Rabin Medical Center institutional review board who waived the requirement for consent.

### 2.1. Statistical analysis

Continuous normally distributed variables are presented as means ± standard deviations (SD). Ordinal and/or non-normally distributed variables are presented by median and interquartile range (IQR). For performance measurement, we assessed correlation using Pearson's r, and concordance was calculated using the concordance correlation coefficient, and plotted using Bland–Altman plots for all. Comparison of measurements was performed using paired T-test. Mean of differences was calculated by taking the sum of difference of each pair of measurements (IC and equation) and dividing by number of pairs. All statistical procedures were performed using R [20].

## 3. Results

A total of 7493 patients were admitted to the ICU during the study period. Of these, 1565 patients had IC measurements performed, for a total of 5847 measurements. After excluding measurement of >5 IC REE and patients with missing anthropomorphic data, 1440 patients with a total of 3573 measurement were included in the final analysis (Fig. 1). For the Faisy and Penn State equations, 1038 patients with 2627 measurements could be assessed. A total of three or more REE measurements were performed on 562 (39%) patients.

For patient with more than one measurement, the mean difference between maximum and minimum measured REE was 490 (±381) kcal. Mean REE was 1957 (±515), with the first measurement's mean (i.e. closest to admission) the lowest, viz. 1891 (±515), while the fifth measurement's mean was 2027 (±495). The differences between measurements were significant ($p < 0.001$). The agreement between the first and last measurement of the same patient was 52% and the correlation was 0.57.

Baseline characteristics of patients are presented in Table 2. Mean age was 58 and 65% were males. Performance of all measurements was assessed using the described methods and is

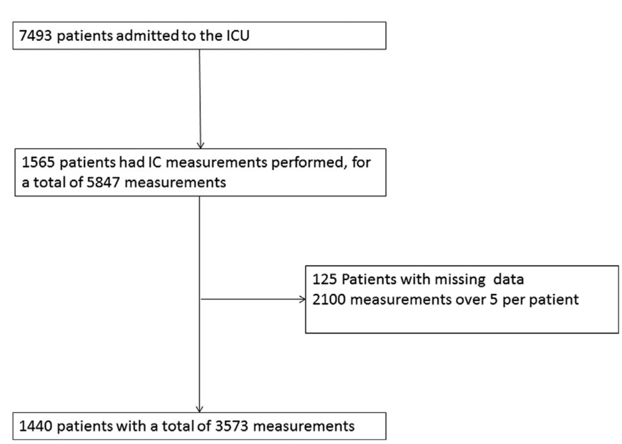


**Fig. 1.** Patient inclusion flowchart.

**Table 2**
Patient characteristics.

| Variable | All measurements | Unique patients |
|---|---|---|
| N | 3573 | 1440 |
| Age | 58.02 (18.70) | 57.77 (18.85) |
| Male gender | 2309 (64.6) | 930 (64.6) |
| Weight | 80.16 (18.84) | 79.74 (18.70) |
| Height (m) | 1.70 (0.09) | 1.70 (0.09) |
| BSA ($m^2$) | 1.90 (0.22) | 1.90 (0.22) |
| BMI ($kg/m^2$) | 27.87 (6.62) | 27.61 (6.39) |
| Need for vasopressors | 1407 (39.4) | 552 (38.3) |
| SOFA score | 7.86 (3.3) | 7.88 (3.43) |
| Admission diagnosis[a] | | |
| Cardiovascular | 724 (26.6) | 291 (26.8) |
| Sepsis | 967 (35.6) | 383 (35.3) |
| Surgical | 1215 (44.7) | 483 (44.5) |
| Trauma | 600 (16.8) | 234 (16.2) |
| Burns | 32 (0.9) | 12 (0.8) |
| Respiratory | 849 (31.2) | 334 (30.8) |
| Minute volume (l) | 9.17 (2.30) | 8.84 (2.19) |
| Temperature (C) | 36.57 (1.06) | 36.60 (1.03) |
| REE (kcal) | 1957.02 (514.57) | 1890.97 (506.49) |

[a] Can be multiple. For continuous variables data presented as mean (sd) and discrete variables as n (%). m-meter, kg-kilogram, C-Celsius, kcal-kilocalories, SOFA-sequential organ failure assessment.

presented in Table 3. Equation performance varied according to parameter, with the Faisy equation demonstrating the least mean difference, Harris–Benedict with a correction factor of 1.3 the highest correlation and agreement, while none reached >50% agreement (between 85% and 115%) with measured REE by IC. The difference of all equations was statistically different from IC ($p < 0.001$) except for the Faisy equation ($p = 0.3$). When examining only the first measurement per patient, performance was slightly worse across all parameters, with agreement varying between 34 and 48% (Table 5). Agreement by difference definitions between equations and IC, and under/overestimation (paralleling under-feeding/overfeeding respectively) patterns is presented in Table 4. Further comparison was performed by inspecting Bland–Altman curves (Fig. 2)

## 4. Discussion

In this study, to our knowledge the largest study comparing measured REE to predictive formulas in critically ill patients, we found that predictive equations have low correlation and agreement with IC. In addition, correlation of the first REE measurement to subsequent ones was low, and the early REE was lower than later measurements, demonstrating the dynamic nature of ICU patients' metabolic needs.

Our results confirm many smaller studies [5,21] as well as a systematic review [22] showing a large SD and poor accuracy of predictive equations. Specifically, McClave [21] found that only 31% of the patients were within 95–110% of IC while 21% were below and 48% above these limits in 213 ventilated ICU patients receiving full nutritional support. Walker and Heuberger [23] analyzed the various predictive equations for energy needs and they too found low accuracy, as did Kross [24]. Some equations that showed promise on the original cohort [25] performed worse in validation studies [26].

The main strength of this study lies in its size, i.e. 1440 patients with multiple measurements for each patient, amounting to an order of magnitude larger than some of the other studies. In addition and importantly, multiple measurements allowed us to take into full account the complex, dynamic and variable nature of a patient's ICU course. By contrast, most equations are unable to allow for this, considering the patient to rather be in a static state, thus exposing an inherent flaw in their ability to truly

**Table 3**
Performance metrics of predictive equations, all measurements.

| Equation | Mean of differences | Standard deviation | % Error | % Difference | Correlation | Concordance | Agreement |
|---|---|---|---|---|---|---|---|
| Faisy | **9.02** | 455.91 | 21 | **13** | 0.49 (0.46–0.52) | 0.57 (0.54–0.6) | 0.49 |
| Harris–Benedict[a] | 94.9 | 446.5 | 21 | **13** | **0.54 (0.51–0.56)** | 0.59 (0.57–0.61) | **0.5** |
| Harris–Benedict[b] | −378.62 | 434.41 | 22 | 16 | **0.54 (0.51–0.56)** | 0.39 (0.37–0.42) | 0.34 |
| Ireton-Jones | 26.81 | 461.16 | **20** | **13** | 0.46 (0.44–0.49) | 0.52 (0.49–0.54) | 0.49 |
| Jolliet | 99.26 | 542.04 | 24 | 14 | 0.51 (0.49–0.54) | **0.62 (0.6–0.64)** | 0.44 |
| Mifflin-St. Jeor | −438.39 | **431.97** | 24 | 17 | 0.54 (0.52–0.57) | 0.35 (0.32–0.37) | 0.3 |
| Penn state | −207.57 | 453.93 | 20 | 14 | 0.51 (0.48–0.54) | 0.54 (0.51–0.57) | 0.44 |
| 25 kcal/kg | 47.08 | 557.74 | 24 | 15 | 0.36 (0.33–0.39) | 0.52 (0.49–0.54) | 0.42 |

Best performing equation in category is in bold.
[a] With a correction factor of 1.3.
[b] No correction factor.

**Table 4**
Agreement of equations with measured REE.

| Equation | 85%–115% agreement | Less than 85% (underfeeding) | More than 115% (overfeeding) | 95%–105% agreement | 75%–125% agreement |
|---|---|---|---|---|---|
| Faisy | 0.49 | 0.21 | 0.3 | 0.17 | 0.72 |
| Harris–Benedict[a] | 0.5 | 0.15 | 0.35 | 0.18 | 0.72 |
| Harris–Benedict[b] | 0.34 | 0.58 | 0.07 | 0.11 | 0.6 |
| Ireton-Jones | 0.49 | 0.2 | 0.31 | 0.18 | 0.74 |
| Jolliet | 0.44 | 0.22 | 0.34 | 0.15 | 0.66 |
| Mifflin-St. Jeor | 0.3 | 0.64 | 0.05 | 0.09 | 0.55 |
| Penn State | 0.44 | 0.4 | 0.16 | 0.15 | 0.7 |
| 25 kcal/kg | 0.42 | 0.24 | 0.34 | 0.15 | 0.66 |

[a] With a correction factor of 1.3.
[b] No correction factor.

**Table 5**
Performance metrics of predictive equations, first measurements (n = 1440).

| Equation | Mean of Differences | Standard Deviation | % Error | % Difference | Correlation | Concordance | Agreement |
|---|---|---|---|---|---|---|---|
| Faisy | **63.66** | 461.48 | 24 | 13 | 0.46 (0.41–0.51) | 0.57 (0.54–0.6) | 0.47 |
| Harris–Benedict[a] | 157.18 | 449.14 | 23 | **13** | 0.52 (0.48–0.55) | 0.59 (0.57–0.61) | **0.48** |
| Harris–Benedict[b] | −315.47 | 434.66 | 22 | 15 | 0.52 (0.48–0.55) | 0.39 (0.37–0.42) | 0.38 |
| Ireton-Jones | 91.05 | 467.16 | 23 | **13** | 0.42 (0.38–0.46) | 0.52 (0.49–0.54) | **0.48** |
| Jolliet | 159.05 | 544.53 | 26 | 15 | 0.5 (0.46–0.54) | **0.62 (0.6–0.64)** | 0.42 |
| Mifflin-St. Jeor | −373.75 | **430.37** | 23 | 16 | **0.53 (0.49–0.56)** | 0.35 (0.32–0.37) | 0.34 |
| Penn State | −147.68 | 470.33 | **22** | 14 | 0.46 (0.41–0.51) | 0.54 (0.51–0.57) | 0.45 |
| 25 kcal/kg | 102.61 | 549.74 | 26 | 15 | 0.36 (0.32–0.41) | 0.52 (0.49–0.54) | 0.42 |

Best performing equation in category is in bold.
[a] With a correction factor of 1.3.
[b] No correction factor.

assess metabolic needs in critically ill patients. While more advanced equations such as Faisy [4] incorporate respiratory data such as minute volume, they nevertheless do not outperform others.

The study has several limitations. First, it is a single center study. Second, the weight is reported as measured but not ideal. This is also an inherent problem with equations, where weight has different definitions and is subject to fluctuations during the stay. In addition, the monitor used in the study (Deltatrac II) is no longer in production so that new devices also need to be validated and are not without fluctuations [27,28]. In addition, it is not clear if assessing energy expenditure leads to improved outcome: only a small RCT showed benefit with IC [10] with support from a retrospective analysis [12]. Results from a further RCT are pending [29]. In addition, different studies used different thresholds for defining agreement, and there is no consensus on what is clinically significant. With this in mind, in addition to choosing a 'main' range (85%–115%), we also present results based on other cutoffs. A 15% difference would amount to a 300 kcal difference on a 2000 kcal target. In a large RCT examining permissive underfeeding [30] the mean group difference was 464 kcal – such a deviation would suggest significant overlap between "underfed" and "standard feeding" groups. Predictive equations' accuracy is influenced by several metabolic factors (sepsis or surgical status, medications, temperature, renal replacement therapy). Thus they might be more or less accurate in specific clinical situation.

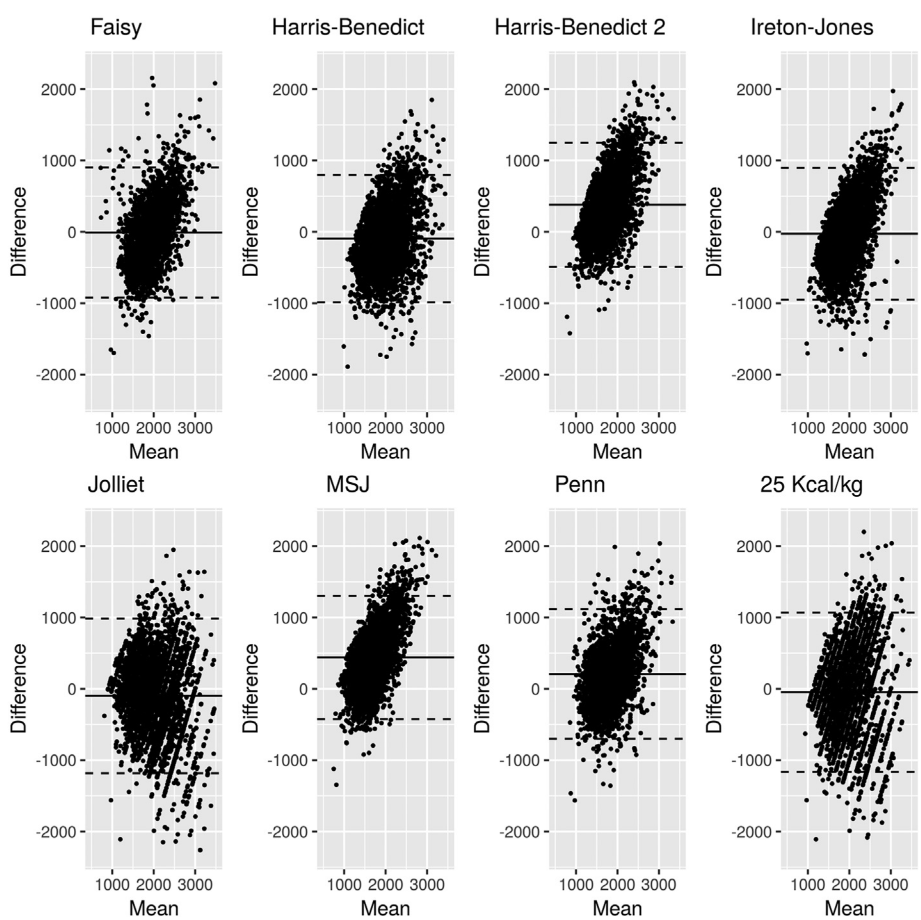


**Fig. 2.** Bland Altman curves of each equation: 'x' axis marks mean of measurements (IC and predicted REE), and 'y' axis as their difference.

Despite all of the above, predictive formulas remain in common use in daily practice as well as in clinical trials dealing with energy requirements of critically ill patients [30,31], so inaccuracies in equations might be carried forward and distort results of RCTs. Recently, the use of VCO2 as derived from the ventilator as a means to calculate REE has been reported, with better accuracy than the predictive equations [32,33] but still not matching that which is obtained by indirect calorimetry [34]. Future studies will need to determine how measuring VCO2 compares to different IC devices.

Finally, recent position papers [1] and reviews [35] suggest that the time has come to recognize the problems in the use of predictive equations, a conclusion which is supported by this study. The way forward, it seems, is more widespread usage of indirect calorimetry with the focus on technological innovations that will make its use easier and more available, possibly with integration to ventilators, or developing and validating measurements based on VCO2.

### *4.1. Conclusions*

In this study, the level of accuracy of the formulae did not exceed 50% in ICU patient. Thus, these equations should not be used in place of indirect calorimetry when assessing nutritional requirements in this population. Future studies are needed to determine the role of measuring only VCO2 and specific IC devices.

## Conflict of interest

All authors, none to declare.


## Funding

None.


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