ARTICLE IN PRESS

Clinical Nutrition (■■■■) ■, ■■■–■■■

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ORIGINAL ARTICLE

Validation of predictive equations for resting energy expenditure in adult outpatients and inpatients☆

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Received 11 December 2006; accepted 7 September 2007

KEYWORDS
Resting energy expenditure;
Predictive equation;
Outpatient;
Inpatient;
Indirect calorimetry;
Validation

Summary
Background & aims: When individual energy requirements of adult patients cannot be measured by indirect calorimetry, they have to be predicted with an equation. The aim of this study was to analyze which resting energy expenditure (REE) predictive equation was the best alternative to indirect calorimetry in adult patients.
Methods: Predictive equations were included when based on weight, height, gender and/or age. REE was measured with indirect calorimetry. The mean squared prediction error was used to evaluate how well the equations fitted the REE measurement.
Results: Eighteen predictive equations were included. Indirect calorimetry data were available for 48 outpatients and 45 inpatients. Also a subgroup of 42 underweight patients (BMI < 18.5) was analyzed. The mean squared prediction error was 233–426 kcal/d and the percentage of patients with acceptable prediction was 28–52% for adult patients depending on the equation used. The FAO/WHO/UNU (1985) equation including both weight and height had the smallest prediction error in adult patients (233 kcal/d), outpatients (182 kcal/d), inpatients (277 kcal/d) as well as underweight patients (219 kcal/d).

☆Conference (poster) presentation: ESPEN 2006, Istanbul, Turkey, P0254.

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doi:10.1016/j.clnu.2007.09.001

Please cite this article as: Weijs PJM, et al. Validation of predictive equations for resting energy expenditure in adult outpatients and inpatients. *Clin Nutr* (2007), doi:10.1016/j.clnu.2007.09.001

Conclusions: The REE of adult outpatients, inpatients and underweight patients can best be estimated with the FAO/WHO/UNU equation including weight and height, when indirect calorimetry is not available.

Introduction

Adequate nutritional therapy requires the estimation of energy requirements of adult patients in order to prevent undernutrition and overnutrition. Energy requirements of adult patients can be assessed by indirect calorimetry. Indirect calorimetry provides reliable information about current resting energy expenditure (REE). Possible increases in energy expenditure due to illness are included in the REE measurement. In most chronic conditions, the REE is normal or slightly increased (~10%) and in acute conditions it is normal to increased (0–50%).[1]

Predictive equations have usually been developed in healthy subjects, based on regression analysis of body weight, height, gender and age as independent variables and measured REE by indirect calorimetry as dependent variable.[2,3] Others have developed different equations per gender[4] and for gender and age groups[5,6] or for BMI groups.[2] One of the few equations that has been developed for adult patients is the Ireton-Jones equation.[7]

Several authors have validated REE predictive equations in healthy subjects[2,8] and in acutely ill patients.[9,10] However, only a few authors have validated a predictive equation in a heterogeneous group of adult patients.[7,11] And no publications could be retrieved which validated a range of predictive equations in an adult mixed patient group. Especially equations derived from relatively large populations of healthy subjects might be of use, but have not been validated in adult patients.[2,5]

While a fixed factor, like 30 kcal/kg, has been a very useful rule of thumb, the present electronic dietetic dossier of outpatients and inpatients (in the Netherlands) allows any REE predictive equation to be incorporated. As part of evidence-based practice, we had to systematically investigate which REE predictive equation would be best to use for the whole patient group.

In this retrospective analysis, the most practical, precise and accurate REE predictive equation for adult patients was sought. Therefore, first the literature was reviewed for REE predictive equations that were of practical use. Secondly these REE predictive equations were validated in outpatients, inpatients and a subgroup of underweight patients with indirect calorimetry data.

Patients and methods

Patients

Adult patients with complete data on weight, height, gender, age, and indirect calorimetry were included. Between July 2002 and April 2005, 48 outpatients and 45 inpatients with heterogeneous background were measured and recorded. These patients were referred for indirect calorimetry when patient energy requirements were unclear, i.e. when patients received total enteral or parenteral nutrition for a longer period of time, when weight development of the patient was unexplained, to evaluate the nutritional therapy or to validate intake measurements. All procedures were in accordance with ethical standards of the institution.

Indirect calorimetry and antropometry

The indirect calorimetry measurements were performed with the Deltatrac I metabolic monitor (Datex-Engstrom Division, Helsinki, Finland), which was calibrated every day before use. Measurements were standardized by internal guidelines. The patient was in supine position and awake. Measurement conditions were semi-standardized conditions that comply with indirect calorimetry measurements in clinical practice. Patients had no feeding several hours before measurement, and had not been physically active. Measurements were performed in standard neutral hospital room temperature. A canopy was placed over the head of the patient. Oxygen consumption and carbon dioxide production was measured and energy expenditure was calculated by the Weir formula.[12] Acceptable coefficient of variation was 10%. The measurements took place for at least 30 min. If repeated measurements were available, only the first measurement was included. Body weight was measured using a calibrated electronic stand-up scale (Seca Alpha, Hamburg, Germany). Gender, age and height of the patient were self-reported.

REE predictive equations

Pubmed was used for a systematical search for publications on Mesh-derived keys 'energy metabolism', 'basal metabolism' and 'indirect calorimetry' and additional terms ('predict*', 'estimat*', 'equation*' and 'formula*') in every possible combination. Applied limitations were 'english language' and 'humans' and age of 18 years and over. More references were obtained by screening publications cited (snowball method). Equations were included when based on gender, age, body weight and/or height only and had to be developed for use in adults. Equations were excluded when based on body composition measurements, and equations aimed at specific target groups (one ethnic group, one sex, only age over 65, etc.) as well as equations developed for critical ill patients.

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For each patient, the REE was predicted for all equations in kcal per day and compared to measured REE. The actual body weight at the time of the indirect calorimetry measurement was used for this calculation. For reference also, a fixed factor of 30 kcal/kg was added. Since this value estimates total energy expenditure instead of REE, the predicted value was divided by 1.3.

Table 1 Number of outpatients and inpatients per diagnosis or reason for indirect calorimetry.

Diagnosis or reason for indirect calorimetry measurement	Outpatients	Inpatients
Inflammatory bowel disease	15	6
Anorexia/chronic underweight	7	8
Coeliac disease	10	2
Neurologic disease	2	6
Overweight	5	1
Short bowel	2	4
Head and neck cancer	2	4
Acute infection		4
Large gastro intestinal surgery		3
Graft versus host illness	1	2
Lung disease	2	
Diabetes mellitus		2
Irritable bowel disease with short bowel	1	1
Thyroid disease	1	
Chronic infection		1
Pulmonary hypertension		1

Statistics

Patient group characteristics have been analyzed by independent samples *T*-test. The mean squared prediction error (MSPE) was used to indicate how well the model predicted in our dataset.[13,14] The concordance correlation coefficient (CCC) was used to show precision and bias of predictive equations.[15] The CCC is a corrected version of the correlation coefficient. The correlation coefficient is a measure of precision. The CCC is calculated by multiplying precision by accuracy. Accuracy is based on the deviation from the line of identity when two methods are plotted on the *x*- and *y*-axes.

A prediction between 90% and 110% of REE measured was considered as acceptable prediction, a prediction below 90% of REE measured was classified as underestimation and a prediction above 110% of REE measured was classified as overestimation. The percentage of patients that had REE predicted within ±10% of REE measured was considered a measure of accuracy on an individual level.[16] The mean percentage difference between REE predicted and measured was considered a measure of accuracy on a group level. Data were analyzed using SPSS 12.0, MSPE with Excel, and CCC with MedCalc version 8.0.2.0.

Results

Table 1 shows the number of outpatients and inpatients per diagnosis or reason for indirect calorimetry measurement. Table 2 shows group characteristics per gender. BMI was significantly lower for inpatients compared to outpatients ($p = 0.022$), but body weight was not significantly different ($p = 0.108$). Outpatients and inpatients were not evenly distributed across BMI groups. The whole patient group included 42 (45%) underweight patients (BMI < 18.5; 17

Table 2 Group characteristics.

Gender	*n*	Age (years)	Weight (kg)	Height (cm)	BMI (kg/m^2)	REE* (kcal/d)	REE (kcal/kg d)
All patients (outpatients and inpatients combined)							
M	34	47.7±17.0[†]	69.4±24.2	181.6±8.3	21.2±8.5	1694±268	26.0±6.4
F	59	43.4±16.8	60.3±23.5	167.8±7.5	21.5±8.4	1396±325	24.7±5.5
All	93	45.0±16.9	63.6±24.0	172.8±10.2	21.4±8.4	1505±336	25.2±5.9
Outpatients							
M	9	50.4±12.7	67.6±15.1	183.8±8.5	20.0±4.3	1591±227	24.1±4.1
F	39	40.3±15.0	67.5±25.1	167.5±7.8	24.0±8.7	1471±312	23.2±4.8
All	48	42.2±15.0	67.5±23.4	170.6±10.1	23.3±8.2	1494±300	23.4±4.7
Inpatients							
M	25	46.8±18.4	70.0±27.0	180.8±8.2	21.6±9.6	1730±276	26.7±7.0
F	20	49.3±18.8	46.3±11.1	168.3±6.9	16.5±4.6	1248±304	27.5±5.7
All	45	47.9±18.4	59.5±24.3	175.2±9.8	19.3±8.1	1516±374	27.1±6.4
Underweight patients							
M	13	42.3±19.3	52.9±6.1	183.6±8.0	15.7±1.6	1610±255	30.7±5.5
F	29	45.3±17.6	44.2±7.3	168.5±6.6	15.5±2.1	1221±239	27.9±4.7
All	42	44.4±18.0	46.9±8.0	173.2±9.9	15.6±1.9	1341±302	28.7±5.1

*REE, resting energy expenditure.
[†]Mean±S.D.

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Table 3 REE predictive equations.

Reference	Referred to as	Comments
Equations based on large populations		
FAO/WHO/UNU[5]	FAOw	6 gender- and age-specific equations, including weight
	FAOwh	6 gender- and age-specific equations, including weight and height
Schofield et al.[17]	Schow	6 gender- and age-specific equations, including weight
	Schowh	6 gender- and age-specific equations, including weight and height
UK Department of Health[6]	UK1991	8 gender- and age-specific equations including weight
Henry[18]	HenryW	6 gender- and age-specific equations, including weight
	HenryWH	6 gender- and age-specific equations, including weight and height
Cole et al.[19]	Cole	1 exponential equation including weight, height and age (for BMI 18.5–30)
	ColeOB	1 exponential equation including weight, height and age (for BMI > 18.5)
Predictive equations based on medium to small populations		
Harris and Benedict[20]	HB1919	2 gender-specific equations, including weight, height and age
Roza and Shizgal[4]	HB1984	2 gender-specific equations, including weight, height and age
Muller et al.[2]	Muller	1 equation including weight, age and gender
	MullerBMI	4 BMI-specific equations including weight, age and gender (and height for BMI 18.5–30)
Owen et al.[21,22]	Owen	2 gender-specific equations, including weight
Mifflin et al.[23]	Mifflin1	1 or 2 equations including weight, height, age and gender
	Mifflin2	2 gender-specific equations, including weight, height and age (simplified factors)
De Luis et al.[24]	DeLuis	2 gender-specific equation, including weight, height and age
Bernstein et al.[25]	Bernstein	2 gender-specific equation, including weight, height and age

outpatients and 29 inpatients) and 15 (16%) obese patients (BMI > 30; 12 outpatients and 3 inpatients). The obese group was not considered large and representative enough to draw conclusions. REE per kg body weight was significantly higher for inpatients compared to outpatients ($p = 0.002$). REE in kcal per day was not significantly different between inpatients and outpatients ($p = 0.754$).

Table 3 shows the 18 REE predictive equations that were included into the study.

Figure 1 shows the bias as percentage of REE measured for FAOwh, HB1984, Mifflin1 and 30 kcal/kg versus REE measured (kcal/d). There appeared to be an overestimation for low REE values and an underestimation of high REE values.

Figure 2 shows the MSPE, Figure 3 shows the bias as percentage difference between prediction and measurement and Figure 4 shows the accepted predictions as percentage of patients. It is shown that the FAO/WHO/UNU equation,[5] using both weight and height as variables (referred to as FAOwh equation), had the smallest MSPE of all 18 equations. This was consistent across outpatients, inpatients and the subgroup of underweight patients. The revised Harris–Benedict equation[4] had very similar or slightly higher MSPE values. Several other equations had prediction errors not more than 25 kcal/d above the lowest value; however, none were as consistent as the FAOwh equation. Especially when also percentage bias (Fig. 3), accepted predictions (Fig. 4) and CCC (data not shown) were considered. The CCC was 0.73 (range 0.62–0.81; precision $0.74 \times$ accuracy 0.98) for FAOwh. Most predictive equations had CCC values between 0.8 and 0.6, meaning that most predictions were moderately precise and accurate. Predictive equations that were based on relatively obese populations appeared to have slightly worse MSPE and CCC values, however this was not a consistent finding (e.g. Mifflin1 equation).

In general, the percentage of patients that had an acceptable prediction was only about 50%. In outpatients, the HB1984 equation predicted as high as two-thirds of the group within 10% of indirect calorimetry measurement; however, the same equation had only one-third of the inpatients predicted well. For inpatients and the subgroup of underweight patients the Mifflin1 equation appeared a good alternative.

The mean difference between REE predicted and measured, expressed as percentage, was very small for the FAOwh equation (−1.0%). Across patient groups this bias remained small for FAOwh, as well as the HB1984 equation. For most equations bias increased especially in the underweight group.

For the fixed factor of 30 kcal/kg, there was a large underestimation of REE for underweight patients.

Discussion

This retrospective analysis shows that the FAO/WHO/UNU equation,[5] including weight and height, is the best

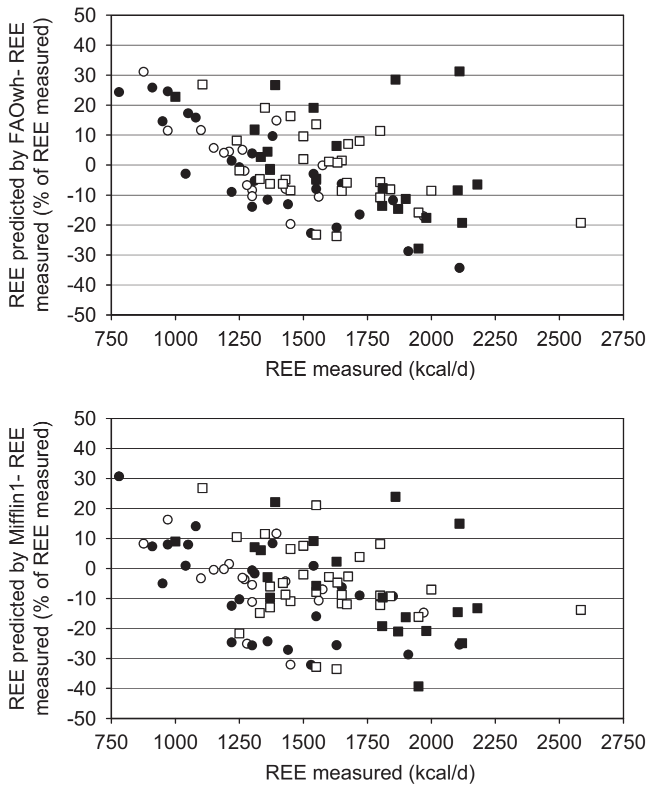

Figure 1 Percentage difference between REE predicted by FAOwh, HB1984, Mifflin1 and 30 kcal/kg versus REE measured with indirect calorimetry (kcal/d) for outpatients (open symbols) and inpatients (filled symbols) that were underweight (BMI < 18.5; circles) or normal weight, overweight, obese (BMI ≥ 18.5; squares).

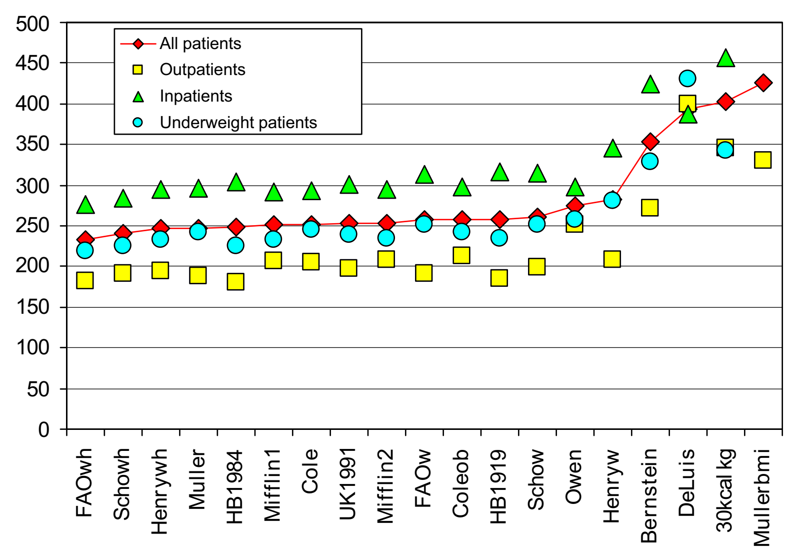

Figure 2 Mean squared prediction error (kcal/d) for all patients (♦), outpatients (■), inpatients (▲) and underweight subgroup (●) for 18 REE predictive equations and 30 kcal/kg.

predictive equation for adult outpatients and inpatients. It is also the best equation for underweight patients. The revised Harris–Benedict equation[4] is a good alternative. However, for inpatients and underweight patients, the Mifflin equation might be considered because of a relatively high percentage of patients that can be predicted well.

We demonstrated that all predictive equations for REE are rather inaccurate for individual patients. The REE of only half the patients is estimated within 10% of the measured REE. Inpatients were particularly difficult to predict, at the most 40% of patients were predicted well (by FAOwh). Thus, when available,

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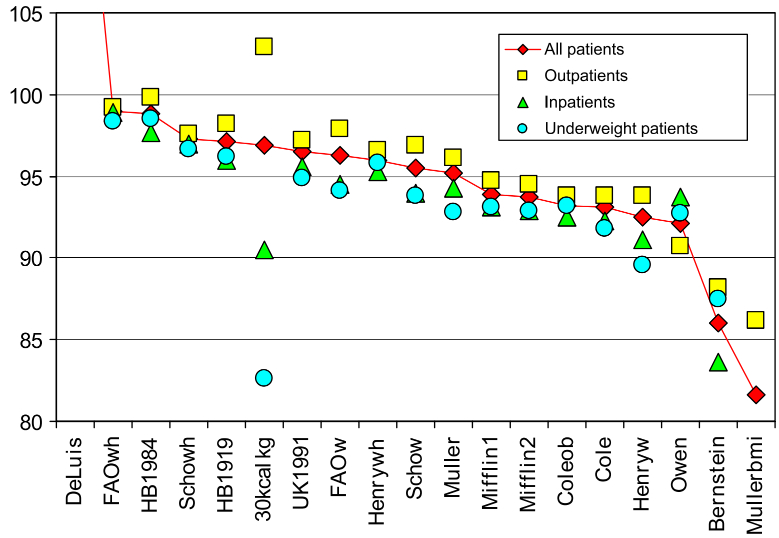

Figure 3 Bias as mean percentage REE predicted of REE measured (REE measured = 100%) for all patients (♦), outpatients (■), inpatients (▲) and underweight subgroup (●) for 18 REE predictive equations and 30 kcal/kg.

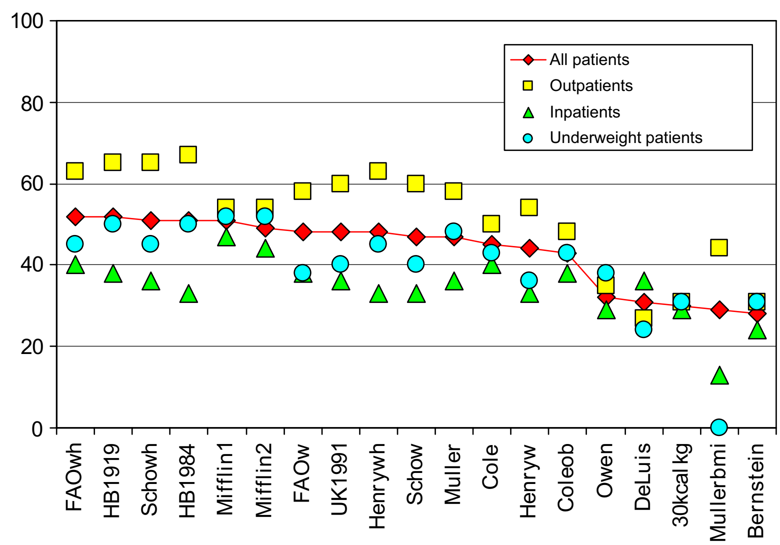

Figure 4 Percentage of patients (%) with acceptable REE predictions for all patients (♦), outpatients (■), inpatients (▲) and underweight subgroup (●) for 18 REE predictive equations and 30 kcal/kg.

measuring REE is the best option in individual patient care.[16,26]

The range of predictive equations shows a prediction error ranging from 233 to 426 kcal/d, which is about 16–28% of REE. This is a large error, considering nutritional therapy of a patient should be close to requirement, in order to avoid undernutrition as well as overnutrition of patients.[27]

Part of the explanation why this heterogeneous patient group cannot be predicted well, could be the metabolic status of the patients that were actually measured for REE because they were not responding adequately to nutritional therapy. However, from a group of control subjects (data not shown), we obtained only slightly higher percentages of subjects predicted well. Therefore, metabolic status per se does not appear to be an important explanation for the performance of REE predictive equations.

The difference in prediction error between inpatients and outpatients (300 kcal/day versus 200 kcal/day) and the percentage of patients predicted well (1/3 versus 2/3) might in part be explained by different body composition. This is not simply due to a BMI below 18.5, since this group had intermediate values (Figures 2 and 4). Although we did not measure body composition in this study, inpatients most likely had a lower amount of muscle mass and body fat and a relatively high percentage (metabolically active) organ mass. This is in line with the observed high REE value in kcal/kg body weight for inpatients. Figure 3 shows that bias from indirect calorimetry is more explained by choice of REE predictive equation than by patient group.

According to a systematic review of Frankenfield et al.,[16] four predictive equations were identified as commonly used: Harris and Benedict,[20] FAO/WHO/UNU,[5] Owen et al.[21,22] and

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Mifflin et al.[23] The Mifflin et al. equation[23] showed the smallest error in estimating REE in healthy non-obese and obese subjects.[8,16] The Mifflin equation is based on a relatively obese population. This equation had the highest percentage of inpatients, and also underweight patients, predicted well. However, the prediction error and especially the bias from measured was much higher than for FAOwh and HB1984.

The original Harris and Benedict equation[8] is the oldest equation still in use and the most evaluated equation. Roza and Shizgal[4] provided a revised Harris–Benedict equation, based on data published by Harris and Benedict between 1919 and 1935. The revised Harris–Benedict equation is not frequently found in the literature. The Harris–Benedict equation is suggested to overestimate basal metabolism[18]; according to Daly et al.[28] even by 10–15%. In underweight patients, Ahmad et al.[29] found REE to be underestimated by the Harris–Benedict equation.[20] Since 5 out of 12 patients were mechanically ventilated, critically ill patients,[29] this might be attributed to an increased metabolic rate as a consequence of illness. We found no apparent underestimation of REE with HB1984 in our underweight patients, who had a similar BMI to the study of Ahmad et al.[29] Müller et al.[2] found HB1919 to overestimate underweight subjects, but not normal weight, overweight and obese subjects. In obese critically ill patients Glynn et al.[10] found the Harris–Benedict equation to overestimate REE, especially above a BMI of 40 kg/m^2. Frankenfield et al.[30] proposed that the Harris–Benedict equation was fair to use upto a BMI of 40 kg/m^2. It has been suggested to use adjusted body weight for obese subjects when using the Harris–Benedict equation.[11,31] It is unclear however which adjusted body weight to use for the REE calculation. We investigated the use of different body weight adjustments (for fixed factor, FAOwh, and HB1984; data not shown); however, the prediction error and the percentage of patients predicted well was always the same or lower compared to the use of actual body weight. Others have indeed concluded that the Harris–Benedict equation should be used with the actual body weight.[8,9,32] We used the actual body weight and REE predictions were only overestimated by about 4% in obese patients and 1.5% underestimated in the underweight patients. Frankenfield et al.[8] found comparable results in healthy subjects (below BMI 40).

The FAO/WHO/UNU equation[5] has not been validated for patients and no individual accuracy data are available.[16] Based on validation in healthy subjects, Müller et al.[2] have suggested that the FAOw equation overestimates low REE values and underestimates high REE values, which seems to be in line with our present observations for FAOwh in patients (see Figure 1). The FAOwh equation is considered to overestimate REE in many communities.[18]

Schofield[17] and FAO/WHO/UNU[5] report that height does not significantly contribute to the estimation of REE in healthy subjects (less than 0.1% of the predicted REE value), therefore predictive equations were based on weight only. The Food and Nutrition Board, Institute of Medicine[33] reports that height is a significant factor in predicting total energy expenditure. Especially for underweight patients, the inclusion of height might reduce the prediction error slightly. Although a reduced prediction error was found by introduction of height (FAOwh versus FAOw, etc.), this had no clinical relevance. Unfortunately in our study height was reported by the patients and can therefore be inaccurate compared to measured height. Although this complies with clinical practice this will add to the total level of inaccuracy. Height measurement might further reduce the prediction error.

In clinical practice often fixed factors like 30 kcal/kg are being used. There is very little evidence base for the use of such single factors and the present study shows that the prediction error of 30 kcal/kg is higher than for most predictive equations. For underweight patients, we found an underestimation of 17.4%. The prediction error for 30 kcal/kg increased to 700 kcal/d for obese subjects, with zero patients predicted in the acceptable range and a mean prediction of 33% above the measurement. Therefore, a fixed factor should be avoided, especially in underweight and obese adult patients.

In conclusion, the FAOwh and HB1984 equations are the most practical and relatively accurate equations that can be used to predict REE in adult outpatients, inpatients and also for underweight patients, when indirect calorimetry is not available. The prediction error is almost half the value for 30 kcal/kg, which suggests that implementation of the FAOwh equation may substantially improve (evidence based) nutritional support in clinical practice. Therefore, we now have implemented this equation in the electronic dietetic dossier in our hospital. This improvement will have to be substantiated in further prospective studies. However, in order to do so, we will also need more evidence for activity factors in order to provide total caloric need. This might help to prevent undernutrition and overfeeding in clinical practice.

Conflict of interest

None of the authors had a conflict of interest.

Acknowledgments

This study was supported by the VU University Medical Center, Amsterdam, the Netherlands.

The contributions of each author of the paper: P.W., H.K., A.D. designed the study, performed literature search, data analysis, and writing of the manuscript; B.M., J.L., R.S., M.B. collected data and provided significant advice on interpretation of results and writing of the manuscript; D.K. provided significant statistical advice.

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Please cite this article as: Weijs PJM, et al. Validation of predictive equations for resting energy expenditure in adult outpatients and inpatients. *Clin Nutr* (2007), doi:10.1016/j.clnu.2007.09.001