



Applied nutritional investigation

New predictive equations for estimating resting energy expenditure in subjects with normal weight and overweight



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ABSTRACT

Objective: The aim of this study was to develop and validate new predictive equations for estimating resting energy expenditure (REE) in subjects with normal weight and overweight, considering anthropometric parameters as well as raw variables from bioimpedance analysis (BIA).

Methods: Adult participants with normal weight and overweight were recruited and randomly split into calibration and validation groups. Indirect calorimetry (IC) and BIA were performed in all subjects. New predictive equations were developed using the following models: model 1 with age, weight, stature, and body mass index (BMI) as predictors; and model 2: model 1 + raw BIA variables (bioimpedance index and phase angle). The accuracy of the new equations at both the group (bias) and individual (within $\pm 10\%$) levels was tested in the validation group. Three published predictive equations were also compared, with the REE values measured by IC.

Results: A total of 2483 adults were included for developing and validating the new equations. All selected formulas, including the new ones, showed a bias of $<5\%$ in estimating REE at the group level. Accuracy at the individual level was slightly higher for the new equations, especially for the equation based on raw BIA variables (men = 70.3%; women = 72.3%).

Conclusions: Compared to the equations in the literature, the new equations showed good accuracy at both the group and individual levels, with a slight improvement in individual accuracy for the formula including raw BIA variables. However, future research is required to verify the role of the raw BIA variables in predicting REE in subjects with normal weight and overweight.

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Introduction

Basal energy expenditure measurement is obtained under total inactivity and controlled research conditions [1]. Resting energy expenditure (REE) refers to the energy measured after an overnight fast (at least 10–12 h), with the subject lying supine and completely at physical and mental rest in a thermoneutral environment [1]. As such, REE is the main component of daily energy expenditure (60–70%) [2], resulting in an important parameter in the assessment of nutritional status, and it can be measured by direct (heat exchange) or indirect calorimetric (gas exchange) techniques [3]. Based on the literature, indirect calorimetry (IC) is

considered the reference method for the measurement of REE [4], requiring standardized conditions and a correct procedure to analyze the data to reduce possible estimation errors in clinical practice [5,6]. Additionally, because of the time required and the high cost of the device, it is difficult to routinely measure REE by IC in clinical settings.

As previously reported, predictive equations are commonly used as an alternative method for estimating REE. The equations are generally developed for sex, age, body weight, stature, and ethnicity [7–12], and some of them have been recently formulated for diseases [13]. Based on the literature, the Harris & Benedict (HB) [14], Schofield [15], and Food and Agriculture Organization/World Health Organization/United Nations University (FAO/WHO/UNU) [16] equations are frequently validated in healthy adults. In particular, the FAO/WHO/UNU equation has been adopted for estimating energy requirements in many countries around the world, while the Schofield equation has been used for estimating REE for the Italian population, as reported by Livelli di Assunzione di

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Riferimento di Nutrienti ed energia per la popolazione italiana (LARN) [17].

In addition to the individual characteristics (age, weight, and stature), many authors have also developed predictive equations using different body composition parameters, in particular fat-free mass (FFM) derived from dual x-ray absorptiometry or bioimpedance analysis (BIA) [18,19]. However, in the literature, the results are still controversial about the inclusion of FFM and its role in the improvement in REE prediction, especially owing to the different equations used to estimate FFM [20].

Recently, we evaluated the inclusion of raw BIA variables, such as the bioimpedance index (BI-index), which is a direct expression of FFM, and the phase angle (PhA), related to body cell mass [21], for predicting REE in patients with obesity [12] and Crohn's disease [13]. The results of these studies [12,13] showed that raw BIA variables could improve the prediction power, but only to a small extent.

To the best of our knowledge, there are no data regarding the use of raw BIA variables (BI-index and PhA) for estimating REE in subjects with normal weight and overweight. Therefore, the aims of the present study were the following: to develop new predictive equations for estimating REE in Italian subjects with normal weight and overweight by using different models (the anthropometric parameters as predictors and both anthropometric and raw BIA variables as predictors); to evaluate the accuracy of the new equations and some of the most commonly used equations; and finally, to assess whether the prediction power of the regression could improve by the inclusion of raw BIA variables into the model.

Materials and methods

This is a retrospective analysis of data on REE collected from a cohort of 2483 subjects at the Department of Clinical Medicine and Surgery, Federico II University Hospital, in Naples, Italy, from May 2005 to May 2019.

Eligible criteria included both sexes, aged ≥ 18 y, with a body mass index (BMI) between 18.5 and 29.9 kg/m² and with no evidence of the following comorbidities: the presence of active inflammatory diseases, dysthyroidism, type 2 diabetes mellitus, pregnancy, lactation, or daily use of prescription medications or drugs known to influence energy metabolism. The study was conducted in accordance with the Declaration of Helsinki, and it was approved by the local Ethics Committee of Federico II University.

All measurements were performed early in the morning after a fasting period of 8 to 10 h according to standardized conditions. We excluded REE data from the analysis if the respiratory quotient was outside the expected range (0.75–0.95) and when measured REE was ± 3 standard deviations outside the mean REE.

Anthropometry

Body weight and stature were measured to the nearest 0.1 kg and 0.5 cm, respectively, and then BMI was calculated as body weight expressed as kilograms divided by the square of stature reported in meters. The measurements were

performed by a platform beam scale with a built-in stadiometer (Seca 709; Seca, Hamburg, Germany), and the subjects wore light clothes and no shoes.

Bioimpedance analysis

BIA is a portable, non-invasive, easy-to-use, and inexpensive method that is widely used in clinical practice for assessing body composition [18]. The measurements were performed at 50 kHz (Human Im Plus II, DS Medica) at room temperature (22–25°C), on the non-dominant side of the body, in the postabsorptive state, after voiding, and with the subject in the supine position for 20 min. The measuring electrodes were placed on the anterior surface of the wrists and ankles, and the injecting electrodes were placed on the dorsal surface of the hands and feet.

Specifically, BIA measures impedance (Z), which is the opposition of the body to an alternating current resulting from resistance (R) and reactance (Xc), while the PhA is identified as the arctangent of the Xc to R ratio [21]. The BI-index was calculated as the ratio of stature²/resistance (cm²/Ω).

Indirect calorimetry

To measure REE, IC using a canopy system (Vmax 29 and Vmax Encore, Sensor Medics, Anaheim, CA, USA) was used [22]. On the day before measurement, all participants were instructed to avoid vigorous physical activity and to abstain from caffeine and nicotine. For fertile women, the measurement was performed during the follicular phase to avoid any potential effects of the menstrual cycle [5,6].

The instrument was routinely checked by burning ethanol, while oxygen and carbon dioxide analyzers were calibrated on the test day using nitrogen and standardized gases (mixtures of nitrogen, carbon dioxide, and oxygen). After an overnight fast (at least 12 h) and at an ambient temperature of 22–25°C, all subjects laid down on a bed in a quiet environment for a 15-min adaptation period, and then, oxygen consumption and carbon dioxide production were measured for 45 min, excluding the first 5 min. Energy expenditure was calculated using the abbreviated Weir's formula, neglecting protein oxidation [23].

REE was estimated using the following predictive equations for subjects with normal weight: HB [14], Schofield [15], and FAO/WHO/UNU equations [16]. Then, the accuracy of the new predictive equations at both the group and individual levels was calculated and compared with those equations.

Statistical analyses

Statistical analyses were performed using IBM SPSS (version 25, Chicago, IL, USA). All data are presented as the mean \pm SD, and significance was defined as $P < .05$. As reported in Table 1, the subjects were randomly assigned to the calibration or validation subset in such a way that the ratio between sexes remained constant [12]. The Kolmogorov-Smirnov test and the Shapiro-Wilk test were used to examine whether variables were normally distributed.

Unpaired *t* tests were used to compare data between the sexes, whereas multivariate linear regression analysis was used to develop the new predictive equations, considering the measured REE by IC as the dependent variable. We generated 2 models:

1. Model 1: age, sex, weight, stature, and BMI as predictors
2. Model 2: model 1 + BIA variables (BI-index and PhA) as predictors

The coefficient of determination (R^2) and standard error of the estimate (SEE) were considered for the evaluation of the predictive power of the formulas. The regression equations resulting from the calibration group were applied to the validation group.

Table 1

Characteristics of all sample, calibration group, and validation group

		All sample (n = 2483)		Calibration group (n = 1485)		Validation group (n = 998)	
		M (n = 805)	F (n = 1678)	M (n = 477)	F (n = 1008)	M (n = 321)	F (n = 677)
Age	y	40.7 \pm 18.4	32.2 \pm 14.4	40.8 \pm 18.4	32.0 \pm 13.9	40.5 \pm 17.9	31.7 \pm 14.1
Weight	Kg	68.8 \pm 11.1*	59.9 \pm 9.5	68.5 \pm 10.8*	60.1 \pm 9.3	69.3 \pm 10.8*	60.1 \pm 9.2
Stature	Cm	172 \pm 7*	161 \pm 6	172 \pm 7*	161 \pm 6	172 \pm 8*	161 \pm 6
BMI	kg/m ²	23.2 \pm 2.9	23.0 \pm 3.2	23.2 \pm 2.9	23.1 \pm 3.2	23.2 \pm 2.9	23.0 \pm 3.1
BI-index	cm ² /ohm	60.1 \pm 9.3*	44.3 \pm 6.5	59.7 \pm 9.1*	44.3 \pm 6.4	61.1 \pm 9.4*	44.2 \pm 6.4
PhA	Degrees	6.62 \pm 1.23	6.10 \pm 0.91	6.64 \pm 1.25	6.11 \pm 0.89	6.65 \pm 1.18	6.16 \pm 0.98
MREE	kcal/d	1628 \pm 274*	1355 \pm 198	1621 \pm 274*	1360 \pm 195	1640 \pm 264*	1354 \pm 199
RQ		0.847 \pm 0.05	0.845 \pm 0.05	0.848 \pm 0.05	0.845 \pm 0.05	0.847 \pm 0.05	0.846 \pm 0.05

BI-index, bioimpedance index; BMI, body mass index; F, female; M, male; MREE, measured resting energy expenditure; PhA, phase angle; RQ, respiratory quotient.

Data are expressed as mean \pm SD.

* $P < 0.05$ ANOVA between sexes.

Table 2

Linear correlation between MREE, individual characteristics, and BIA variables according to sex in all sample

	M (n = 805)	F (n = 1678)	All (n = 2483)
Age	-0.443	NS	-0.057
Weight	0.668	0.570	0.680
Stature	0.527	0.358	0.597
BMI	0.402	0.446	0.405
BI-index	0.614	0.448	0.673
PhA	0.284	0.165	0.302

All variables are significantly correlated with REE unless otherwise specified. BI-index, bioimpedance index; BMI, body mass index; F, female; M, male; MREE, measured resting energy expenditure; NS, not significant; PhA, phase angle

As a measure of accuracy at the group level, the mean difference between the predicted REE (PREE) and measured REE (MREE) and bias (i.e., the average percent difference) was considered. Bias was found to be acceptable if it was within $\pm 5\%$ [24,25].

The percentage of subjects with a PREE within 90% to 110% was used as a measure of accuracy at the individual level. Therefore, values lower than 90% were classified as underprediction, whereas values higher than 110% were classified as overprediction. The root mean square error was used to define the predictions obtained with these models. Bland-Altman plots were used to estimate the limits of agreement [26] between the PREE-MREE differences vs the mean PREE-MREE values.

Results

A total of 2483 subjects (805 men and 1678 women) were included in this analysis. Table 1 summarizes the anthropometric parameters, raw BIA variables, and MREE data for the entire sample as well as for both the calibration and validation groups. We found that BMI, respiratory quotient, and PhA did not vary between the sexes, whereas age, body weight, stature, MREE, and BI-index significantly differed.

Pearson's linear correlation (Table 2) showed that the MREE was directly correlated with individual characteristics and raw BIA variables in both sexes. In contrast, the MREE was significantly

associated with age in men ($r = -0.443$, $P < 0.001$) but not in women ($r = -0.015$, $P = 0.527$). Body weight displayed the strongest correlation with MREE, followed by the BI-index, in both sexes (men: $r = 0.668$, $P < 0.001$; women: $r = 0.570$, $P < .001$).

The new predictive equations were derived from the calibration group. Multiple regression analysis was performed to formulate the new equation of REE using the different predictors (models 1 and 2).

- Model 1 (sex, age, weight, stature, and BMI)

$$\text{REE(kcal/d)} = 70.4 + (12.1 \times \text{weight}) + (3.83 \times \text{stature}) + (139 \times \text{sex}[1]) - (1.82 \times \text{age})$$

$$(R^2 = 0.687; \text{SEE} = 133\text{kcal/d})$$

- Model 2 (Model 1 + PhA + BI-Index)

$$\text{REE(kcal/d)} = 104.0 + (9.39 \times \text{weight}) + (20.9 \times \text{PhA}) + (1.99 \times \text{stature}) + (66.5 \times \text{sex}[1]) + (6.47 \times \text{BI-index}[2]) - (1.41 \times \text{age})$$

$$(R^2 = 0.699; \text{SEE} = 125\text{kcal/d})$$

where for sex, women = 0 and men = 1 and BI-index = stature²/resistance at 50 kHz (cm²/ohm).

Validation of the new predictive equations (group level and individual level)

To assess the accuracy of the new predictive equations, 998 subjects were randomly assigned to the validation group (321 men and 677 women). The PREE, the difference between the PREE and MREE, the percent bias (accuracy at the group level), and the root mean square error for both the new equations and selected equations are described in Table 3 and Table 4.

We found that both equations 1 and 2 showed a bias of $<5\%$ in both sexes. Specifically, the mean bias of equation 1 was 1.3% and

Table 3

Evaluation of selected predictive equations in 321 men based on differences Predicted-Measured, percentage of accuracy, Bias and Root Mean Square Error.

REE predictive equations	PREEkcal/d	Difference PREE-MREEkcal/d	Bias*%	Max negativeerror%	Max positiveerror%	RMSEkcal/d
HB	1609 \pm 241	-31 \pm 207	-0.9	-30.2	49.2	167
Schofield	1696 \pm 150	56 \pm 200	5.2	-24.7	53.1	165
FAO/WHO/UNU	1692 \pm 154	52.9 \pm 200	4.9	-25.2	52.5	164
Equation (1)	1635 \pm 160	-4.8 \pm 196	1.3	-27.3	47.9	151
Equation (2) [†]	1640 \pm 168	0.78 \pm 186	1.1	-27.6	39.1	144

FAO/WHO/UNU, Food and Agriculture Organization/World Health Organization/United Nations University; HB, Harris and Benedict; MREE, measured resting energy expenditure; PREE, predicted resting energy expenditure; REE, resting energy expenditure; RMSE, root mean square error
Average REE measured with indirect calorimetry = 1640 \pm 264 kcal/d.

*Mean percentage error between predictive equations and measured value.

[†]Including bioimpedance index and phase angle.

Table 4

Evaluation of selected predictive equations in 677 women based on differences Predicted-Measured, percentage of accuracy, Bias and Root Mean Square Error.

REE predictive equations	PREE	Difference PREE-MREE kcal/d	Bias*%	Max negativeerror%	Max positiveerror%	RMSEkcal/d
HB	1379 \pm 115	25 \pm 174	3.5	-33.5	41.5	141
Schofield	1348 \pm 111	-5.7 \pm 162	1	-30.8	34.0	129
FAO/WHO/UNU	1362 \pm 112	8.8 \pm 162	2.1	-29.9	35.0	129
Equation (1)	1358 \pm 126	4.4 \pm 161	1.7	-29.9	35.6	127
Equation (2) [†]	1354 \pm 126	1.2 \pm 155	1.3	-27.0	39.2	120

FAO/WHO/UNU, Food and Agriculture Organization/World Health Organization/United Nations University; HB, Harris and Benedict; MREE, measured resting energy expenditure; PREE, predicted resting energy expenditure; REE, resting energy expenditure; RMSE, root mean square error
Average REE measured with indirect calorimetry = 1353 \pm 198 kcal/d.

*Mean percentage error between predictive equations and measured value.

[†]Including bioimpedance index and phase angle.

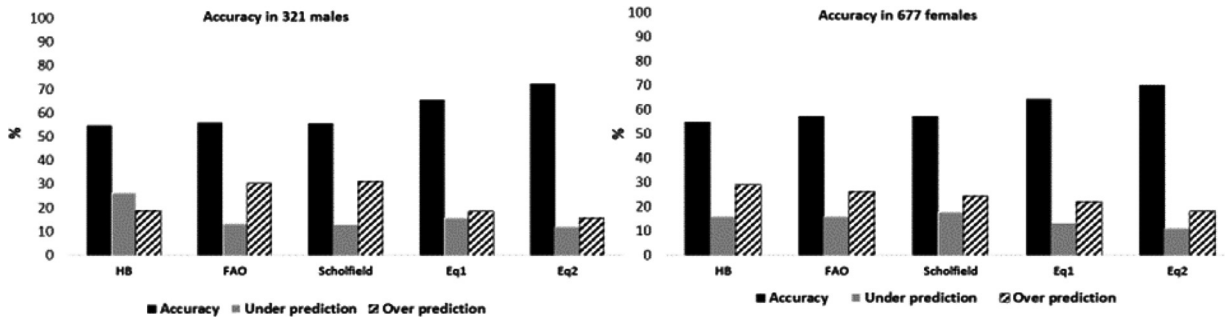


Fig. 1. Prediction accuracy within $\pm 10\%$. Accuracy of prediction equations for measurements of resting energy expenditure within $\pm 5\%$ using each equation in 321 men and 677 women, respectively. HB, Harris and Benedict; FAO, Food and Agriculture Organization; Eq 1, equation generated by model 1; Eq 2, equation generated by model 2.

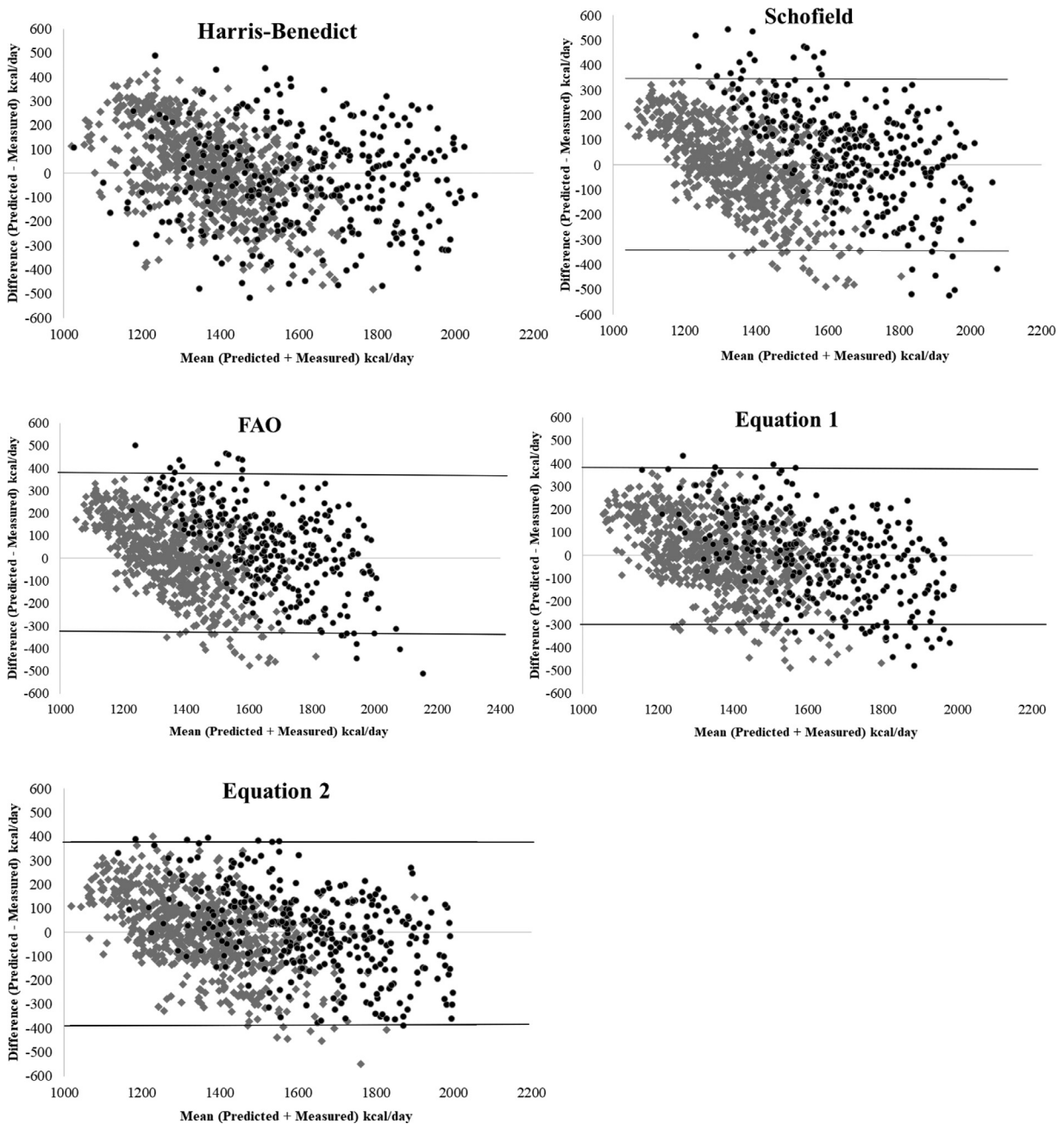


Fig. 2. Bland-Altman plots. Bland-Altman plots between differences and mean predicted-measured resting energy expenditure using the selected equations and the new predictive equations (equations 1 and 2) in men (●) and in women (◊). The dotted lines represent 2 SDs from the mean (limits of agreement).

that of equation 2 was 1.1% in men, whereas in women, it was 1.7% and 1.3% for equation 1 and equation 2, respectively. Among the selected equations from the literature, we found that the HB equation in men and the Schofield equation in women were the most accurate at the group level (mean bias -0.9 and 1 , respectively).

Regarding the accuracy at the individual level, the percentages of participants with a PREE within $\pm 10\%$ of the MREE for the new and other predictive equations are reported in Figure 1. The new equations reported the highest accuracy in both men (equation 1: 65.6%; equation 2: 72.3%) and women (equation 1: 64.3%; equation 2: 70.3%) when compared to the other equations. Most of them tended to overpredict REE in both sexes, except for the HB equation, which underpredicted REE in men

Bland-Altman Plots of PREE-MREE differences

The Bland-Altman plots of predicted-measured REE differences vs mean predicted-measured REE obtained by all equations are reported in Figure 2. There is good agreement for both the HB equation and the new equations, especially in men.

Discussion

This study aimed to develop and validate new predictive equations for subjects with normal weight and overweight and then to assess the accuracy of the most commonly used REE predictive equations. Our findings showed that body weight was the main determinant of REE, followed by the BI-index, whereas age showed an inverse correlation with REE. Interestingly, the new equations gave a good accuracy prediction at both the group and individual levels in both sexes, resulting in slightly higher accuracy using the formula including the raw BIA variables.

Previously, we performed the same evaluations in patients with obesity [12], Crohn disease [13], and anorexia nervosa [27], observing that the use of raw BIA variables in the model provided a comparable REE prediction with the model exclusively based on anthropometric variables. As such, we opted to develop new predictive equations including raw BIA variables in subjects with normal weight and overweight, which should be free of any confounding factors related to excessive body weight [12] or diseases [13,27].

Generally, predictive equations for estimating REE provide acceptable results when applied in the population from which they are derived [24]. Currently, the HB, Schofield, and FAO/WHO/UNU equations are the most widely used equations in clinical practice to predict REE in healthy adults [28–30], even if many studies in the literature showed that the accuracy rates of these equations at both the group and individual levels were different, depending on several factors, such as the possible effects of race/ethnicity [31,32].

In a recent study by Bedogni et al [30], the authors investigated the prediction accuracy in a large sample of Italian adults with normal weight and overweight, reporting that accuracy at the group level, assessed by bias, was within $\pm 5\%$ using the HB equation (4%), whereas it was higher with the FAO/WHO/UNU and Schofield equations (FAO/WHO/UNU= 6%; Schofield= 7%). Additionally, in previous studies performed in Italian [9] and Arabic populations [33], the authors found that the bias of these equations was acceptable since it was lower than 5% in both men and women, whereas in Korean adults [34], it was higher (HB = -7.2 ; FAO/WHO/UNU = -5.2 ; Schofield = -5.5%), resulting in an underestimation of REE prediction. Accordingly, our results showed a good prediction at the group level from all considered equations, except for the Schofield equation in men.

Regarding the accuracy at the individual level, the study by Bedogni et al [30] showed that the accuracy was 72% and 73% using the HB equation, 66% and 64% using the FAO/WHO/UNU equation,

and 60% and 65% with the Schofield equation in Italian adults with normal weight and overweight, respectively. Another study [33] found that only the HB equation reached 61% accurate prediction in women, whereas in Korean adults [34], the accuracy rates were higher for both the Schofield and FAO/WHO/UNU equations (66% and 67%, respectively). In our study, the results at the individual level showed that all equations reached at least 60% prediction accuracy in both sexes.

To the best of our knowledge, this is the first study that develops specific equations to predict REE in subjects with normal weight and overweight considering the inclusion of raw BIA variables. A strength of this study is the sample size, which was large enough for subgroup analyses between sexes, although there were more women than men. However, it should be considered that our results may not be extended to other populations.

In conclusion, our results showed that the new REE predictive equations proposed for subjects with normal weight and overweight showed good accuracy at both the group and individual levels, especially those including raw BIA variables. Therefore, the use of population-specific predictive equations is highly recommended for evaluating REE in cases where its measurement, which is the preferred option, is unavailable or unfeasible. Future studies are required to verify the applicability of these equations in subjects with normal weight and overweight and to explore the role of raw BIA variables in the prediction of REE.

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