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How Well Are We Predicting the Resting Energy Expenditure in Underweight to Obese Brazilian Adults?

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Abstract Resting energy expenditure (REE) measurement is costly and rarely feasibly. Alternatively, is easily predicted by predictive equations but accuracy varies across ethnicity, body size and body composition. The purpose was to evaluate the validity of REE predictive equations between adult from Brazil and across body mass index (BMI). We also developed a new equation. It was a cross-sectional observational study in which predicted REE was tested for agreement with indirect calorimetry. Brazilian men and women (n=367) age from 20 to 40 years were analyzed from October 2016 to October 2017. Participants were from underweight to obese (BMI from 17 to 40kg/m^2). REE was measured (mREE) with indirect calorimetry and predicted (pREE) by REE predictive equations. Each equation was compared for accuracy (pREE= ±10%mREE). Bias between mREE and pREE with 95% confidence intervals, Bland-Altman and scatter plots graphs were also analyzed. The root mean squared error measured the performance of the equations. Stepwise multiple-regression analyses were applied for developing a new equation. As a result, the new equation (r^2= 0.46; SEE= 226.92kcal/day) presented a good performance among normal, overweight and obese subjects (51, 51 and 45% of accuracy, respectively). The best performance of REE equations evaluated were from Anjos (39% of accuracy) among underweight subjects; Anjos and Sabounchi among normal weight (38% of accuracy for both) and overweight (53 and 48% of accuracy, respectively) individuals; Anjos and Owens (48 and 44% of accuracy, respectively) among obese subjects. No equation was able to accurately predict REE in 60% of the time and all tended to overestimate. In conclusion, Anjos, Sabounchi and Owens equations showed the best performances. Therefore, all predictive equation presented large individual errors. The new equation had a good performance from normal to obese individuals. However, indirect calorimetry is still necessary for the most accurate information about energy needs.

Keywords: *resting energy expenditure, indirect calorimetry, predictive equations, weight management, body mass index*

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1. Introduction

As recently reported [1,2], the proportion of adults with excess weight has been increasing in high to low-income countries, and ranges from 40 to 50% worldwide [1,2]. In Brazil, a fast increase in adult obesity has been occurring: the latest national survey on nutritional status [3] showed that half of the adults are overweight and 15% are obese. On the other hand, undernutrition still exists in the world, mainly in poverty [4] and in low-income countries such as Brazil [3]. Excess weight and obesity are considered one of the main causes of mortality and metabolic diseases in the modern and affluent world [5] and malnutrition still has a great influence in morbimortality [4]. Therefore, weight management has become a major global health challenge.

Young adults are a large segment of the population in need of weight management. As long-term small inadequacies in energy balance negatively interfere on weight management [6,7], once under and overestimation of energy needs could predispose to the development of malnutrition and obesity-comorbidities, the assessment of energy needs is the first step of a personalized dietary plan. The FAO Reports [8,9] established that the energy requirement should be based on total daily energy expenditure, of which 60 to 80% is represented by resting energy expenditure (REE) [10]. Thus, the energy content of a diet is usually based on the REE.

REE can be measured by indirect calorimetry [7], but the methodology is costly and rarely feasibly in clinical practice. As an alternative, REE is usually and more easily calculated by predictive equations. On the other hand, its accurate determination is a challenge since it relies in the accuracy and bias of the chosen equation and varies across individuals and population groups. In addition, choosing the most adequate equation among the existing ones is another great challenge. The FAO Reports [8,9] provide a set of formulas to estimate REE based on easily assessed parameters (sex, age, body weight, and height) to guide clinicians. Thus, the validation of REE prediction equations is a way to marginally provide utility and information about calculation of energy needs in various populations.

As ethnicity [11,12] and body composition [12,13] play an important role in the variation of REE, they are a central issue in the performance of REE predictive equations. As recently observed by an expert panel from the American Dietetic Association [6], clinicians should be cautious when applying predictive equations to groups of subjects who are underrepresented in development and validation studies, as the application to participants that fall outside of the original sample might not be appropriate resulting in inappropriate REE estimation.

Taking this into account, the accuracy and reliability of REE prediction equations in different populations remain inconsistent and need further validation: the evaluation of usually applied equations has been limited since the majority of the studies were done with Europeans and North Americans, are restricted across body size and body composition, and scarce in young healthy population. As a gap of investigation, studies with Latin American populations are rare.

Therefore, the purpose of the present study was to examine the accuracy and bias of common REE predictive equations when applied in Brazilian adults from underweight to obese to assess the equations 'utility in a population with different body sizes. In addition, three newer equations were evaluated: one with a specific ethnicity fit derivate from a metanalysis [14], another recently developed from a Mexican data base [15], and one developed from Brazilian population [16]. We also developed and validated a new equation.

With this study we pretend to help clinicians in choosing the best REE prediction equations for application in the target population, also in the planning of public health policies and dietary interventions, helping in weigh management and prevention of malnutrition and excess weight.

2. Materials and Methods

This cross-sectional observational study was conducted at the University of São Paulo at Ribeirão Preto, with a group of 367 non-smoker Brazilians (hospital or university staff, under or graduate students), 193 females and 174 males, aged between 20 and 40 years, being 3% of Asian and 9% of African descent. Subjects ranging from underweight to obese without acute or chronic diseases (exception: obesity) were recruited specifically for this study and exclusion criteria were pregnancy, lactation, use of drugs that influence energy metabolism and body composition, menopause, presence of amputation and metal objects in the body as protheses or pacemakers, being on a diet for weight loss, unintentional or intentional weight loss greater than 10% in the last 6 months, and others that could interfere in bioelectrical impedance analysis and indirect calorimetry results.

The study was conducted in accordance to the Declaration of Helsinki and received the approval of the Local Ethical Committee (number: 1076550). All participants provided written informed consent prior to the initiation of the study procedures. Convenience sampling was applied to contact and screen potential candidates: all subjects interested in participating in the research during the study period (from October 2016 to October 2017) and that met the eligibility criteria were evaluated.

This study followed the STROBE guidelines.

The same professional performed all measurements consecutively in a temperature-controlled (23-27°C) room, early in the morning after a fasting period of 12 h with abstention from beverage or foods containing alcohol or caffeine and rigorous physical activity for 36 h prior to evaluation [7,17]. All participants completed health-related interview to ensure adherence to study protocol.

Anthropometric data. Body weight and height were measured in duplicate in light clothing without shoes using a platform beam scale with a built-in stadiometer (FilizolaEletrônica ID 1500, Filizola Corporation) and the mean of the values was used. Nutritional status was defined according to BMI: underweight (BMI<18.5 kg/m^2), normal weight (18.5≤BMI<25 kg/m^2), overweight (25≤BMI<30 kg/m^2), and obese (BMI≥30 kg/m^2).

Body Composition data. Body composition was evaluated by tetra-polar wrist-to-ankle multifrequency bioelectrical impedance spectroscopy (BCM, Fresenius Medical Care) in accordance to published protocol [17]: measurements were carried out on the right side of the body after the volunteer being in supine position for 20 min and data about fat free mass (FFM) and fat mass (FM) were collected.

REE data. REE was measured according to a recommended protocol [7] in a thermoneutral (20-25°C), humidity-controlled (45-55%), and quiet environment and in a supine position using a validated indirect calorimetry system [18] (VO2000, Aerograf). Before starting the test, the device was heated for 30 min and the barometric and gasometric calibration were performed, both automatically and manually using Aerograf software, according to manufacturer's instructions. Subjects laid down on the bed for a 25-min adaptation period, proved to allow accurate REE measures [7]. Afterwards, oxygen consumption and carbon dioxide production were measured for 30 min; the first 5 min were eliminated and REE was calculated from minute-to-minute values averaged over the remaining time of steady state [7] using the Weir equation [19] and reported in kcal/day. Data were excluded from analysis if the respiratory quotient was outside the physiological range (0.70-1.00) and if steady state was less than 15 min. Participants were monitored for activity, hyperventilation, or napping. Fifty participants (25 women) repeated the REE measures on different days with an interval of 3 to 5 days. Mean REE values between days were not significantly different (mean difference = 7 kcal±15; p=0.43), the two measures were highly correlated (r=0.94), and the mean intra-individual coefficient of variation of measured REE (mREE) was 4.7%.

Evaluation of REE predictive equations. The performance of predictive equations commonly applied in clinical practice [8,9,13,20-28] and three new equations [14-16] were analyzed (see Table 1, *supplementary material*). We applied all equations according to the sex, age, weight, height and BMI status. Performance of predicted REE (pREE) and bias between pREE and mREE at group and individual levels were evaluated for the total sample and for each BMI subgroup. The CI95% for mean bias was evaluated. The root mean square error (RMSE) was used to measure how well the equations fitted the mREE at group level. A predictive equation was considered accurate at the individual level if pREE and mREE were within ±10%. Under (pREE<90% mREE) and over predictions (pREE>110% mREE) were also calculated. Bland-Altman plots were used in the total sample to assess agreement at the individual level between pREE and mREE. Correlation between bias of pREE and mREE with BMI were analyzed in total sample by scatter plots.

Table 1. Resting energy expenditure (kcal/day) prediction equation evaluated

REE prediction equation referred to as	Year Developed	Study population	Sex, age or obesity status	Equation[a]
Harris-Benedict [20]	1918	n=239 (136 male, 103 female); mean age: males 27 years, females 32 years; mean body mass index: males 21.4kg/m^2, females 24.4 kg/m^2; healthy north-American; large participation of normal weight females.	Men	66.4730 + 13.7516(W) + 5.0033(H) – 6.7550(A)
			Women	655.0955 + 9.5634(W) + 1.8496(H) – 4.6756(A)
Mifflin-St Jeor [25]	1990	n=498 (251 male, 247 female); mean age: males 44 years, females 45 years; normal weight and obese; white healthy north-American.	Men/Women	9.99(W) + 6.25(H) - 4.92(A) + 166(sex) - 161
Owens [22,23]	1986, 1987	n=104 (60 male, 44 female); mean age: males 38 years, females 35 years; mean body mass index: males 28.2kg/m^2, females 27.8kg/m^2; normal weight and obese; males: healthy white, black and Asian, females: healthy but ethnicity was not stated.	Men	879 + 10.2(W)
			Women	795 + 7.18(W)
Frankenfield#1 [28]	2013	n=337 (94 male, 243 female); age from 18 to 85 years; from underweight to large obese; healthy; 95% Caucasian.	Non-obese men/women	10(W) + 3(H) – 5(A) + 207(sex) + 454
			Obese men/women	10(W) + 3(H) – 5(A) + 244(sex) + 440
Frankenfield#2 [28]			Non-obese men/women	10(W) – 6(A) + 230(sex) + 838
			Obese men/women	10(W) – 5(A) + 274(sex) + 865
FAO/WHO/ONU#1 [8,9]	1985; 2004	Based on data of >114 studies and 7.000 subjects; ~33% female; large range of age and body mass index; healthy adults of varying weights, heights and ages; multiethnic cohort, included a large number of Italian participants.	Men (18 ≤ age < 30)	15.3(W) + 679
			Men (30 ≤ age < 60)	11.6(W) + 879
			Women (18 ≤ age < 30)	14.7(W) + 496
			Women (30 ≤ age < 60)	8.7(W) + 829
FAO/WHO/ONU#2 [8,9]			Men (18 ≤ age < 30)	15.4(W) - 0.27(H) + 717
			Men (30 ≤ age < 60)	11.3(W) + 0.16(H) + 901
			Women (18 ≤ age < 30)	13.3(W) + 3.34(H) + 35
			Women (30 ≤ age < 60)	8.7(W) - 0.25(H) + 865
Livingston-Kohlstadt#1 [27]	2005	Data from Harris-Benedict and Owens data base with additional of 327 new measurements. n=655 (299 male, 356 female); mean age: males 36 years, females 39 years; mean weight: males 96kg, females 90kg.	Men	$293(W)^{0.4330}$ - 5.92(A)
			Women	$248(W)^{0.4356}$ - 5.09(A)
Livingston-Kohlstadt#2 [27]			Men	$246(W)^{0.4473}$
			Women	$196(W)^{0.4613}$
Muller#1 [13]	2004	Data from a German data base. n=1046 (388 male, 658 female); mean age: 44.2 years; mean body mass index: 27.1kg/m^2; from underweight to obese; white healthy subjects.	Total sample men/women	[0.047(W) + 1.009(sex) - 0.01452(A) + 3.21]*239
			BMI<18.5 kg/m^2 men/women	[0.07122(W) - 0.02149(A) + 0.82(sex) + 0.731]*239
			18.5≤BMI<25 kg/m^2 men/women	[0.02219(W) + 0.02118(H) + 0.884(sex) - 0.01191(A) + 1.233]*239
			25≤BMI<30 kg/m^2 men/women	[0.04507(W) + 1.006(sex) - 0.01553(A) + 3.407]*239
			BMI≥30 kg/m^2 men/women	[0.05(W) + 1.103(sex) - 0.01586(A) + 2.924]*239
Muller#2 [13]			Total sample men/women	[0.05192(FFM) + 0.04036(FM) + 0.869(sex) - 0.01181(A) + 2.992]*239
			BMI<18.5 kg/m^2 men/women	[0.08961(FFM) + 0.05662(FM) + 0.667]*239
			18.5≤BMI<25 kg/m^2 men/women	[0.0455(FFM) + 0.0278(FM) + 0.879(sex) - 0.01291(A) + 3.634]*239
			25≤BMI<30 kg/m^2 men/women	[0.03776(FFM) + 0.03013(FM) + 0.93(sex) - 0.01196(A) + 3.928]*239
			BMI≥30 kg/m^2 men/women	[0.05685(FFM) + 0.04022(FM) + 0.808(sex) - 0.01402(A) +2.818]*239

REE prediction equation referred to as	Year Developed	Study population	Sex, age or obesity status	Equation[a]
Henry-Rees [26]	1991	Data derived from people living in tropical regions (many countries). n=1896 (1448 male, 448 female); age from 18 to 30 years (n=1524) and age from 30 to 60 years (n=372).	Men (18 ≤ age < 30)	[0.057(W) - 0.00429(H) + 3.412]*239
			Men (30 ≤ age < 60)	[0.046(W) - 0.00081(H) + 3.277]*239
			Women (18 ≤ age < 30)	[0.042(W) + 0.01546(H) + 0.433]*239
			Women (30 ≤ age < 60)	[0.047(W) + 0.00145(H) + 2.256]*239
Schofield [21]	1985	Formed the base for FAO/WHO/ONU report in 1985. Meta-analyses of 114 studies. From infants to adults; both sex; large presence of Europeans and north-Americans with a low representativeness of other ethnicities.	Men (18 ≤ age < 30)	[0.063(W) + 2.896]*239
			Men (30 ≤ age < 60)	[0.048(W) + 3.653]*239
			Women (18 ≤ age < 30)	[0.062(W) + 2.036]*239
			Women (30 ≤ age < 60)	[0.034(W) + 3.538]*239
Ireton-Jones [24]	1989	Obese hospitalized patients.	Obese men/women	629 – 11(A) + 25(W) - 609
			Non-obese men/women	629 – 11(A) + 25(W)
Sabounchi [14]	2013	Derived from a meta-analysis of 47 studies. Healthy white from 18 to 56 years.	Men (18 ≤ age < 57)	361 + 21.1(FFM) + 4.77(FM)
			Women (18 ≤ age < 57)	360 + 21(FFM) + 4.68(FM)
Anjos [16]	2013	n=529 adults (190 male, 339 female); mean age: males 43 years, females 45 years; mean body mass index: males 25kg/m^2, females 25.4kg/m^2; from underweight to obese; healthy population from a tropical region (only Brazil).	Men	[41.79(W) + 29.86(H) – 11.69(A) – 1884.93]*239
			Women	[37.46(W) + 37.13(H) – 2.92(A) – 3407,09]*239
NEQ [15]	2017	n=100 adults (35 male; 65 female); mean age: 30.1±9.88 years; mean body mass index: 22.1±1.87kg/m^2; only normal weight; healthy population from Mexico	Men	[12.225(H) - 4.135(A) - 243.812]*239
			Women	[12.225(H) – 4.135(A) – 464.033]*239
		n=210 adults (58 male; 152 female); mean age: 39.1±11.2 years; mean body mass index: 31.6±5.35kg/m^2; only overweight and obese (60%); healthy population from Mexico.	Men	[12.114(W) - 6.541(A) + 1094.991]*239
			Women	**[12.114(W) - 6.541(A) + 835.952]*239**

[a] W: weight (kg); H: height (cm); A: age (years); FFM: fat free mass (kg); FM: fat mass (kg); BMI: body mass index (kg/m^2); Sex (Men = 1; Women = 0); obesity status = BMI > 30 kg/m^2.

Development and evaluation of a new REE equation. The sample was randomly split into design (n=184) and validation (n=183) groups and compared with Student's t-test. For the generation of the new equation, correlation analysis (Pearson or Spearman correlation) and scatter plots were used to select the covariates (sex, men = 1 and women = 0; age (years); weight (kg); height (cm); FFM (kg and %); and FM, (kg and %)) that would be entered into the multiple linear regression model to observe the linearity between continuous independent variables and the dependent variable (mREE). The correlation coefficient and the independent association of each covariate were analyzed, demonstrating the collinearity between them. The interactions between the variables were verified; no significant interaction was found. In order to identify the variables, either alone or in combination, with the highest correlations and predictors of mREE, a stepwise multiple regression analysis (α=0.15) was used to predict REE (kcal/day) in the sample. The adjusted coefficient of determination (r^2), the slope (α), and the intercepts (β) were analyzed, and the fit of the model was performed by selecting the best model. For the final fit of the prediction model, the normality of the residuals was tested by observing the plot between the residuals and the predicted values, presenting constant variance and zero mean (application of normal Q-Q plot and Shapiro-Wilk normality test, with p>0.05). The statistical analyses described in the previous paragraph were applied in the evaluation of the new equation.

Statistical analysis. Continuous variables are presented as mean ± SD and minimum and maximum values, and categorical variables as frequencies and percentages. Q-Q plots were applied to analyze whether data were normally distributed. For variables that were not normally distributed, appropriate logarithmic transformations were performed. The Mann-Whitney test was used for differences between males and females, and ANOVA for comparing data between BMI subgroups. Pearson correlation was used to assess the association between pREE and mREE. Statistical significance was considered when p<0.05. Data analysis was performed using MINITAB 2013.

3. Results

Descriptive data are shown in Table 2. Age was similar between sexes. Men had a higher body weight, height, FFM, and FFMI, but FM and FMI were higher in women. Both were classified on average as overweight. REE was greater in men than women, but when corrected for body weight, no difference was observed. Between BMI subgroups, women and men were equally distributed; underweight was an exception due to a greater participation of women. Weight, FM, FMI, and REE were significantly different and increased with increasing BMI classification. However, REE per body weight decreased with increasing BMI classification.

Design and validation groups were similar (see Table 3, *supplementary material*). The new equation was named **Bellafronte-Chiarello**: **REE (kcal/day) = 546.3 + 158.0(sex) + 8.8(weight) (Model R^2 = 0.46; SEE = 226.92)**, weight in kg and sex, men = 1 and women = 0. The equation was derived from simple parameters providing an easily available equation for clinical settings. This equation was unbiased at group level (see Table 4). At individual level, a good performance was found for normal weight, overweight, and obese; underweight subjects presented a low accuracy and a high underestimation rate.

Table 2. Descriptive data for total sample, women, men and per BMI subgroups

	Total sample	Women	Men	BMI < 18.5	18.5 ≤ BMI < 25	25 ≤BMI < 30	BMI ≥30
n	367	193	174	35	115	114	103
%	100	53	47	10 (80% women)	31 (51% women)	31 (50% women)	28 (48% women)
Age (years)	29±4.5 (20-40)	28±4.3 (20-40)	29±4.8 (20-40)	26±3.6 (20-35)^{a}	29±3.9 (20-40)^{b}	29±4.6 (20-40)^{b}	30±4.9 (20-40)^{b}
Weight (kg)	77±19 (39-124)	69±17 (39-116)*	86±17 (45-124)*	48±5.1 (39-60)^{a}	64±9.3 (45-87)^{b}	79±9.9 (59-109)^{c}	98±12 (71-124)^{d}
Height (cm)	170±9.5 (150-194)	163±6.1 (150-181)*	177±6.6 (157-194)*	166±8.3 (153-187)^{a}	170±9.2 (150-192)^{b}	170±9.6 (151-194)^{b}	171±9.7 (150-190)^{b}
BMI (kg/m^2)	27±5.6 (17-40)	26±6.1 (17-40)*	27±5.0 (17-40)*	18±0.49 (17-18)^{a}	22±1.8 (19-24.9)^{b}	27±1.5 (25-29.9)^{c}	34±2.7 (30-40)^{d}
FFM (kg)	44±12 (25-76)	34±4.7 (25-48)*	55±7.8 (37-76)*	34±6.3 (26-51)^{a}	43±12 (26-70)^{b}	46±12 (27-76)^{b}	46±13 (25-76)^{b}
FFM (%)	58±14 (26-97)	51±12 (26-83)*	66±12 (38-97)*	70±8.0 (57-89)^{a}	66±12 (42-97)^{a}	57±12 (35-87)^{b}	47±11 (26-76)^{c}
FFMI (kg/m^2)	15±3.0 (8.9-23)	13±1.6 (8.9-17)*	17±2.2 (12-23)*	12±1.5 (10-16)^{a}	15±2.8 (9.3-22)^{b}	15±3.1 (10-23)^{b}	16±3.2 (8.9-23)^{b}
FM (kg)	33±16 (1.9-83)	35±16 (9.3-83)*	31±16 (1.9-75)*	14±3.8 (4.8-21)^{a}	21±7.3 (1.9-38)^{b}	33±9.5 (11-57)^{c}	52±12 (22-83)^{d}
FM (%)	42±14 (2.9-74)	49±12 (17-74)*	34±12 (2.9-62)*	30±8.0 (11-43)^{a}	34±12 (2.9-58)^{a}	43±12 (13-65)^{b}	53±11 (24-74)^{c}
FMI (kg/m^2)	12±5.8 (0.61-29)	13±6.0 (3.5-29)*	9.7±4.9 (0.61-24)*	5.2±1.5 (1.9-7.8)^{a}	7.6±2.8 (0.61-13)^{b}	12±3.6 (3.5-19)^{c}	18±4.6 (7.1-29)^{d}
mREE (kcal/day)	1323±319 (669-2262)	1178±249 (669-1999)*	1483±312 (822-2262)*	994±221 (669-1405)^{a}	1201±235 (769-1924)^{b}	1359±265 (839-2047)^{c}	1530±331 (917-2262)^{d}
mREE/Weight (kcal/kg/day)	18±3.5 (8.1-28)	18±3.6 (9-28)	18±3.3 (8.1-27)	20±3.9 (13-27)^{a}	19±3.4 (9.9-28)^{b}	17±2.7 (11-24)^{c}	16±4.6 (8.1-22)^{d}

Data presented as mean ± SD (minimum - maximum values). *p < 0.05 female vs male (Mann - Whitney test). Values with different letters in the same row between BMI subgroups columns are significantly different, $p < 0.05$ (ANOVA). BMI: body mass index; FFM: fat free mass; FM: fat mass; FFMI: fat free mass index; FMI: fat mass index; mREE: measured resting energy expenditure by indirect calorimetry.

Table 3. Descriptive and comparative data between design and validation group

	Design Group	Validation Group
n	184	183
% Women	53	52
Underweight	14 W and 3 M	14 W and 4 M
Normal weight	30 W and 27 M	29 W and 28 M
Overweight	30 W and 27 M	29 W and 28 M
Obese	24 W and 29 M	23 W and 28 M
Age (years)	28±4.6 (20-40)	29±4.5 (20-40)
Weight (kg)	77±19 (42-120)	76±18 (39-124)
Height (cm)	170±9.7 (150-194)	170±9.3 (150-194)
BMI (kg/m^2)	27±5.6 (17-39)	26±5.6 (17-40)
FFM (kg)	44±13.2 (25-76)	44±11.4 (26-71)
FFM (%)	58±15 (26-97)	59±14 (27-93)
FFMI (kg/m^2)	15±3.2 (8.9-23)	15±2.8 (10.2-23)
FM (kg)	34±17 (1.9-80)	33±16(4.7-83)
FM (%)	42±15 (3-74)	42±14 (7-73)
FMI (kg/m^2)	12±5.9 (0.6-28)	12±5.6 (1.4-29)
mREE (kcal/day)	1308±325 (669-2175)	1337±313 (723-2262)
mREE/Weight (kcal/kg/day)	18±3.5 (8-27)	18±3.4 (9-28)

Data presented as mean ± SD (minimum – maximum values). No difference was observed between design and validation group (unpaired and parametric student t test, p>0.05). BMI: body mass index; FFM: fat free mass; FM: fat mass; FFMI: fat free mass index; FMI: fat mass index; M: men; mREE: measured resting energy expenditure by indirect calorimetry; W: women.

Table 4. Statistics of the new REE prediction equation (Bellafronte-Chiarello)

Total Validation Group (n = 183)									
pREE (kcal/day)	pREE/mREE	SEE (kcal/day)	Bias (%)[a]	95% CI Bias (%)[b]	RMSE (%)[c]	Under prediction (%)[d]	Accurate prediction (%)[e]	Over prediction (%)[f]	r
1295±208	1.0±0.17	226.92	-0.34±17.19	-3 to 2	17.33	30	46	24	0.69*
Underweight Validation Group (n = 18)									
1011±109	1.0±0.19	56.43	4.51±19.45	-5 to 14	19.44	82	18	0	0.57*
Normal weight Validation Group (n = 57)									
1189±146	1.0±0.17	114.69	-1.34±16.54	-6 to 3	16.45	49	51	0	0.50*
Overweight Validation Group (n = 57)									
1321±143	1.0±0.15	107.97	0.3±15.30	-4 to 4	15.17	21	51	28	0.62*
Obese Validation Group (n = 51)									
1484±165	1.0±0.20	153.28	-1.45±19.74	-7 to 4	19.6	0	45	55	0.49*

Data presented as mean ± SD. r: Pearson correlation coefficient: *p<0.05 pREE vs mREE. [a]Mean percentage error between pREE and mREE: pREE-mREE/ mREE X 100. 95% CI: 95% Confidence Interval. [b]95% CI of difference between pREE and mREE (%): pREE-mREE / mREE x 100 (95% intervals that include zero are unbiased). RMSE: Root mean square prediction error. [c]RMSE (%): pREE-mREE / mREE x 100. [d]The percentage of subjects whose pREE was < 90% of mREE. [e]The percentage of subjects whose pREE was within 10% of mREE. [f]The percentage of subjects whose pREE was > 110% of mREE. REE: resting energy expenditure; mREE: measured resting energy expenditure by indirect calorimetry; pREE: predicted resting energy expenditure by prediction equations; SEE: standard error of the estimate.

The statistics of the REE predictive equations evaluated are shown in Table 5 (total sample) and Table 6, Table 7, Table 8, Table 9 (BMI subgroups). Bland-Altman plots for bias between pREE and mREE in the total sample are presented in Figure 1 (*supplementary material*): large limits of agreement towards overestimation were observed with greater bias in extremes of REE. Scatter plots between pREE and mREE bias with BMI for the total sample are presented in Figure 2 (*supplementary material*): a positive correlation was observed between them. Only for Owens, Livingston-Kohlstadt#2, Muller#2, Anjos, and NEQ equations no correlation was seen (p>0.05).

Table 5. Statistics of REE prediction equations evaluated in total sample (n= 367)

REE prediction equation	**pREE (kcal/day)**	**pREE/mREE**	**Bias (%)[a]**	**95% CI Bias (%)[b]**	**RMSE (%)[c]**	**Under prediction (%)[d]**	**Accurate prediction (%)[e]**	**Over prediction (%)[f]**	**r**
Harris-Benedict	1698±305	1.3±0.25	32.17±24.96	30 to 35	40.70	0.5	16.0	83.5	0.69*
Mifflin-St Jeor	1606±288	1.3±0.24	25.14±23.57	23 to 28	34.44	1.0	28.0	71.0	0.68*
Owens	1510±274	1.2±0.23	17.58±22.66	15 to 20	28.65	7.0	36.0	57.0	0.67*
Frankenfield#1	1688±274	1.3±0.25	31.76±24.65	29 to 34	40.18	0.3	18.0	81.7	0.68*
Frankenfield#2	1615±272	1.3±0.23	25.86±23.43	23 to 28	34.87	0.8	26.0	73.2	0.69*
Schofield	1690±327	1.3±0.25	31.23±24.61	29 to 34	39.74	0.5	18.0	81.5	0.69*
FAO/WHO/ONU#1	1699±329	1.3±0.25	31.93±24.77	29 to 34	40.39	0.5	17.0	82.5	0.69*
FAO/WHO/ONU#2	1740±348	1.3±0.26	35.00±25.76	32 to 38	43.44	0.3	13.0	86.7	0.69*
Henry-Rees	1566±269	1.2±0.23	22.03±22.75	20 to 24	31.64	3.0	27.0	70.0	0.69*
Ireton-Jones	2062±421	1.6±0.35	60.87±35.24	57 to 64	70.31	0.8	05.0	94.2	0.56*
Livingston-Kohlstadt#1	1611±267	1.3±0.23	25.59±23.31	23 to 28	34.60	1.0	27.0	72.0	0.69*
Livingston-Kohlstadt#2	1571±262	1.2±0.23	22.53±22.97	20 to 25	32.15	3.0	30.0	67.0	0.68*
Muller#1	1646±284	1.3±0.24	28.21±23.95	26 to 31	36.98	0.8	22.0	77.2	0.69*
Muller#2	1595±270	1.2±0.23	24.34±23.18	22 to 27	33.58	1.3	27.0	71.7	0.69*
Sabounchi	1396±266	1.1±0.22	9.20±22.23	6.9 to 11	24.09	17.0	41.0	42.0	0.65*
Anjos	1398±256	1.1±0.21	9.10±21.12	6.9 to 11	22.72	14.0	45.0	41.0	0.60*
NEQ[g]	1753±298	1.3±0.22	32.29±22.37	30 to 35	39.25	0.3	14.0	85.0	0.59*

Data presented as mean ± SD. r: Pearson correlation coefficient: *p<0.05 pREE vs mREE. [a]Mean percentage error between pREE and mREE: pREE-mREE/ mREE X 100. 95% CI: 95% Confidence Interval. [b]95% CI of difference between pREE and mREE (%): pREE-mREE / mREE x 100 (95% intervals that include zero are unbiased). RMSE: Root mean square prediction error. [c]RMSE (%): pREE-mREE / mREE x 100. [d]The percentage of subjects whose pREE was < 90% of mREE. [e]The percentage of subjects whose pREE was within 10% of mREE. [f]The percentage of subjects whose pREE was > 110% of mREE. [g]For NEQ equation,underweight subjects were not evaluated as the equations developed are only for normal weight to obese subjects. REE: resting energy expenditure; mREE: measured resting energy expenditure by indirect calorimetry; pREE: predicted resting energy expenditure by prediction equations.

Table 6. Statistics of REE prediction equations evaluated in underweight subgroup (n=35)

REE Prediction equation	pREE (kcal/day)	pREE/mREE	Bias (%)[a]	95% CI Bias (%)[b]	RMSE (%)[c]	Under prediction (%)[d]	Accurate prediction (%)[e]	Over prediction (%)[f]	r
Harris-Benedict	1333±117	1.4±0.27	39.34±27.06	30 to 90	47.53	0.0	11.0	89.0	0.54*
Mifflin-St Jeor	1265±153	1.3±0.25	31.77±25.52	23 to 41	40.52	0.0	20.0	80.0	0.54*
Owens	1192±126	1.2±0.25	24.65±24.50	16 to 33	34.75	3.0	31.0	66.0	0.45*
Frankenfield#1	1348±144	1.4±0.27	40.71±27.16	31 to 50	48.72	0.0	14.0	86.0	0.53*
Frankenfield#2	1263±137	1.3±0.25	31.79±25.36	23 to 41	39.92	0.0	26.0	74.0	0.52*
Schofield	1249±142	1.3±0.26	30.48±26.16	21 to 39	39.92	0.0	29.0	71.0	0.48*
FAO/WHO/ONU#1	1253±142	1.3±0.26	30.91±26.35	22 to 40	40.37	0.0	29.0	71.0	0.47*
FAO/WHO/ONU#2	1286±169	1.3±0.27	34.25±27.22	25 to 44	43.50	0.0	26.0	74.0	0.47*
Henry-Rees	1213±98	1.3±0.25	26.95±25.18	18 to 36	36.64	0.0	31.0	69.0	0.54*
Ireton-Jones	1505±143	1.6±0.37	58.79±37.20	46 to 72	69.29	3.0	6.0	91.0	0.31*
Livingston-Kohlstadt#1	1256±136	1.3±0.25	31.04±25.29	22 to 40	39.81	0.0	26.0	74.0	0.52*
Livingston-Kohlstadt#2	1219±134	1.3±0.25	27.30±25.36	19 to 26	37.01	3.0	29.0	68.0	0.47*
Muller#1	990±308	1.0±0.27	14.20±27.37	-08 to 11	27.01	43.0	29.0	28.0	0.48*
Muller#2	1147±218	1.2±0.26	19.02±25.68	10 to 28	31.66	14.0	23.0	63.0	0.45*
Sabounchi	1134±130	1.2±0.24	19.12±24.78	10 to 27	30.25	11.0	25.0	64.0	0.40*
Anjos	1081±131	1.1±0.22	13.02±22.56	5.2 to 20	25.45	14.0	39.0	47.0	0.37*

Data presented as mean ± SD. r: Pearson correlation coefficient: *$p<0.05$ pREE vs mREE. [a]Mean percentage error between pREE and mREE: pREE-mREE/ mREE X 100. 95% CI: 95% Confidence Interval. [b]95% CI of difference between pREE and mREE (%): pREE-mREE / mREE x 100 (95% intervals that include zero are unbiased). RMSE: Root mean square prediction error. [c]RMSE (%): pREE-mREE / mREE x 100. [d]The percentage of subjects whose pREE was < 90% of mREE. [e]The percentage of subjects whose pREE was within 10% of mREE. [f]The percentage of subjects whose pREE was > 110% of mREE. REE: resting energy expenditure; mREE: measured resting energy expenditure by indirect calorimetry; pREE: predicted resting energy expenditure by prediction equations.

Table 7. Statistics of REE prediction equations evaluated in normal weight subgroup (n=115)

REE Prediction equation	pREE (kcal/day)	pREE/mREE	Bias (%)[a]	95% CI Bias (%)[b]	RMSE (%)[c]	Under prediction (%)[d]	Accurate prediction (%)[e]	Over prediction (%)[f]	r
Harris-Benedict	1500±203	1.3±0.24	32.44±24.09	28 to 37	40.34	1.0	16.0	83.0	0.48*
Mifflin-St Jeor	1483±212	1.3±0.23	26.50±2335	22 to 31	35.25	2.0	23.0	75.0	0.49*
Owens	1402±205	1.2±0.22	19.65±22.36	15 to 24	29.69	8.0	29.0	63.0	0.46*
Frankenfield#1	1564±204	1.3±0.24	33.61±24.18	29 to 38	41.35	1.0	16.0	83.0	0.48*
Frankenfield#2	1482±196	1.3±0.23	26.57±23.23	22 to 31	35.22	2.0	23.0	75.0	0.47*
Schofield	1531±220	1.3±0.24	30.65±24.34	26 to 35	39.07	2.0	19.0	79.0	0.48*
FAO/WHO/ONU#1	1537±221	1.3±0.25	31.21±24.51	27 to 36	39.61	2.0	18.0	80.0	0.47*
FAO/WHO/ONU#2	1582±247	1.3±0.26	34.88±25.91	30 to 40	43.38	1.0	16.0	83.0	0.47*
Henry-Rees	1422±171	1.2±0.22	21.62±21.77	18 to 26	30.61	4.0	24.0	72.0	0.48*
Ireton-Jones	1868±264	1.6±0.34	60.31±33.75	54 to 67	69.03	1.0	3.0	96.0	0.28*
Livingston-Kohlstadt#1	1490±201	1.3±0.23	27.22±23.34	23 to 32	35.79	2.0	22.0	76.0	0.47*
Livingston-Kohlstadt#2	1459±202	1.2±0.23	24.56±22.88	20 to 29	33.50	3.0	23.0	74.0	0.47*
Muller#1	1512±187	1.3±0.23	29.24±23.07	25 to 34	37.18	2.0	18.0	80.0	0.47*
Muller#2	1485±193	1.3±0.23	26.84±22.63	23 to 31	35.04	1.0	24.0	75.0	0.48*
Sabounchi	1346±239	1.1±0.22	15.03±22.56	11 to 19	26.56	7.0	38.0	55.0	0.43*
Anjos	1281±184	1.1±0.20	9.52±20.67	6 to 13	22.21	14.0	38.0	48.0	0.47*
NEQ	1599±206	1.4±0.24	36.95±24.61	32 to 41	44.32	0.30	12.0	87.7	0.34*

Data presented as mean ± SD. r: Pearson correlation coefficient: *$p<0.05$ pREE vs mREE. [a]Mean percentage error between pREE and mREE: pREE-mREE/ mREE X 100. 95% CI: 95% Confidence Interval. [b]95% CI of difference between pREE and mREE (%): pREE-mREE / mREE x 100 (95% intervals that include zero are unbiased). RMSE: Root mean square prediction error. [c]RMSE (%): pREE-mREE / mREE x 100. [d]The percentage of subjects whose pREE was < 90% of mREE. [e]The percentage of subjects whose pREE was within 10% of mREE. [f]The percentage of subjects whose pREE was > 110% of mREE. REE: resting energy expenditure; mREE: measured resting energy expenditure by indirect calorimetry; pREE: predicted resting energy expenditure by prediction equations.

Table 8. Statistics of REE prediction equations evaluated in overweight subgroup (n=114)

REE Prediction equation	pREE (kcal/day)	pREE/mREE	Bias (%)[a]	95% CI Bias (%)[b]	RMSE (%)[c]	Under prediction (%)[d]	Accurate prediction (%)[e]	Over prediction (%)[f]	r
Harris-Benedict	1721±237	1.3±0.21	29.42±20.85	26 to 33	36.00	0.0	17.0	83.0	0.64*
Mifflin-St Jeor	1632±221	1.2±0.20	22.75±19.73	19 to 26	30.05	0.0	26.0	74.0	0.65*
Owens	1526±224	1.1±0.19	19.95±20.68	11 to 18	28.74	4.0	40.0	36.0	0.64*
Frankenfield#1	1711±209	1.3±0.21	28.93±20.56	25 to 33	35.44	0.0	17.0	83.0	0.65*
Frankenfield#2	1645±203	1.2±0.20	23.96±19.82	20 to 28	31.04	0.0	25.0	75.0	0.65*
Schofield	1727±242	1.3±0.21	29.88±21.11	26 to 34	36.54	0.0	17.0	83.0	0.63*
FAO/WHO/ONU#1	1736±242	1.3±0.21	35.42±24.34	27 to 34	42.77	0.0	15.0	85.0	0.63*
FAO/WHO/ONU#2	1782±273	1.3±0.22	33.78±22.00	30 to 38	40.26	0.0	11.0	89.0	0.64*
Henry-Rees	1594±197	1.2±0.19	20.06±19.31	16 to 24	27.79	3.0	32.0	65.0	0.64*
Ireton-Jones	2170±288	1.7±0.35	65.14±35.23	59 to 72	73.98	1.0	8.0	91.0	0.20*
Livingston-Kohlstadt#1	1642±205	1.2±0.20	23.66±19.75	20 to 27	30.76	1.0	25.0	74.0	0.64*
Livingston-Kohlstadt#2	1600±201	1.2±0.19	20.48±19.23	17 to 24	28.03	2.0	31.0	67.0	0.64*
Muller#1	1657±200	1.2±0.20	24.93±20.38	21 to 29	32.15	0.0	25.0	75.0	0.65*
Muller#2	1624±190	1.2±0.20	22.41±19.56	19 to 26	29.69	2.0	27.0	71.0	0.64*
Sabounchi	1436±255	1.1±0.18	7.40±18.03	4 to 11	19.24	15.0	48.0	37.0	0.66*
Anjos	1426±199	1.1±0.17	7.20±17.02	4 to 10	18.83	11.0	53.0	36.0	0.64*
NEQ	1730±225	1.3±0.20	30.20±20.84	26 to 34	36.63	0.0	15.0	85.0	0.34*

Data presented as mean ± SD. r: Pearson correlation coefficient: *$p<0.05$ pREE vs mREE. [a]Mean percentage error between pREE and mREE: pREE-mREE/ mREE X 100. 95% CI: 95% Confidence Interval. [b]95% CI of difference between pREE and mREE (%): pREE-mREE / mREE x 100 (95% intervals that include zero are unbiased). RMSE: Root mean square prediction error. [c]RMSE (%): pREE-mREE / mREE x 100. [d]The percentage of subjects whose pREE was < 90% of mREE. [e]The percentage of subjects whose pREE was within 10% of mREE. [f]The percentage of subjects whose pREE was > 110% of mREE. REE: resting energy expenditure; mREE: measured resting energy expenditure by indirect calorimetry; pREE: predicted resting energy expenditure by prediction equations.

Table 9. Statistics of REE prediction equations evaluated in obese subgroup (n=103)

REE Prediction equation	pREE (kcal/day)	pREE/mREE	Bias (%)[a]	95% CI Bias (%)[b]	RMSE (%)[c]	Under prediction (%)[d]	Accurate prediction (%)[e]	Over prediction (%)[f]	r
Harris-Benedict	1959±283	1.3±0.29	32.49±28.85	27 to 38	43.36	1.0	16.0	83.0	0.49*
Mifflin-St Jeor	1831±235	1.2±0.27	24.04±26.65	19 to 29	35.79	2.0	37.0	61.0	0.49*
Owens	1718±262	1.2±0.26	23.16±32.75	11 to 21	40.11	10.0	44.0	46.0	0.48*
Frankenfield#1	1916±239	1.3±0.28	29.83±27.70	24 to 35	40.62	0.0	26.0	74.0	0.48*
Frankenfield#2	1847±227	1.3±0.26	25.16±26.42	20 to 30	36.39	1.0	32.0	67.0	0.50*
Schofield	1976±276	1.3±0.28	33.59±27.92	28 to 39	43.59	0.0	16.0	84.0	0.51*
FAO/WHO/ONU#1	1990±273	1.3±0.28	34.58±28.13	29 to 40	44.49	0.0	15.0	85.0	0.51*
FAO/WHO/ONU#2	2024±299	1.4±0.29	36.71±29.02	31 to 42	46.71	0.0	14.0	86.0	0.52*
Henry-Rees	1814±225	1.2±0.26	22.97±26.20	18 to 28	34.75	2.0	40.0	58.0	0.49*
Ireton-Jones	2343±263	1.6±0.36	57.52±36.20	50 to 65	67.87	0.0	4.0	96.0	0.50*
Livingston-Kohlstadt#1	1831±218	1.2±0.26	24.11±25.98	19 to 29	35.36	1.0	35.0	64.0	0.50*
Livingston-Kohlstadt#2	1784±215	1.2±0.26	20.95±25.74	16 to 26	33.09	5.0	39.0	56.0	0.43*
Muller#1	1868±221	1.3±0.28	26.89±27.94	21 to 32	38.68	2.0	26.0	72.0	0.47*
Muller#2	1788±213	1.2±0.26	21.34±26.20	16 to 26	33.70	3.0	40.0	57.0	0.49*
Sabounchi	1502±268	1.0±0.24	10.67±24.03	-3 to 6	23.60	33.0	36.0	29.0	0.60*
Anjos	1613±222	1.1±0.24	09.45±24.67	05 to 14	26.05	16.0	48.0	36.0	0.58*
NEQ	1970±243	1.3±0.24	31.13±24.30	26 to 36	39.04	0.0	18.0	82.0	0.58*

Data presented as mean ± SD. r: Pearson correlation coefficient: *$p<0.05$ pREE vs mREE. [a]Mean percentage error between pREE and mREE: pREE-mREE/ mREE X 100. 95% CI: 95% Confidence Interval. [b]95% CI of difference between pREE and mREE (%): pREE-mREE / mREE x 100 (95% intervals that include zero are unbiased). RMSE: Root mean square prediction error. [c]RMSE (%): pREE-mREE / mREE x 100. [d]The percentage of subjects whose pREE was < 90% of mREE. [e]The percentage of subjects whose pREE was within 10% of mREE. [f]The percentage of subjects whose pREE was > 110% of mREE. REE: resting energy expenditure; mREE: measured resting energy expenditure by indirect calorimetry; pREE: predicted resting energy expenditure by prediction equations.

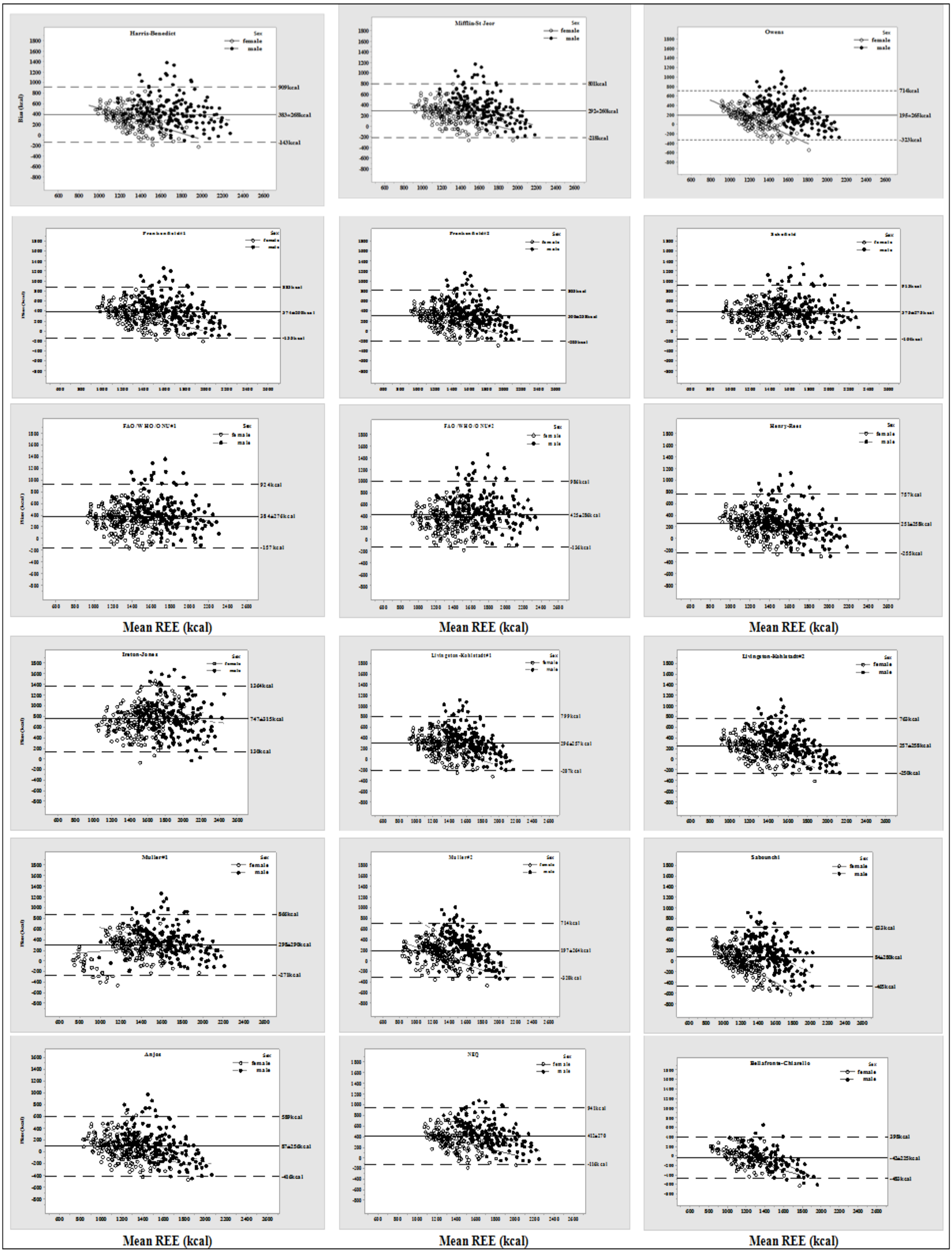

Figure 1. Bland-Altman plots of the bias between REE determined by indirect calorimetry and by sixteen prediction equations against the mean of the two methods. Analysis performed with the total sample. Bias (kcal/d) for each REE prediction equation was determined by subtracting mREE from pREE. The solid black line represents the mean measurement difference and the dashed black lines correspond to the 95% limits of agreement (±2 SD). The gray solid line is the regression line for the measurement bias plotted against the mean of the two methods for female and the gray dashed line for male subjects. Separate plots are presented for each equation. The name of each equation ploted is in the graphic and is referee to as the same named presented in Table 1. For NEQ equation, underweight subjects were not evaluated as the equations developed are only for normal weight to obese subjects. For Bellafronte-Chiarello equation, the equation was evaluated using subjects form validation group (see Table 3)

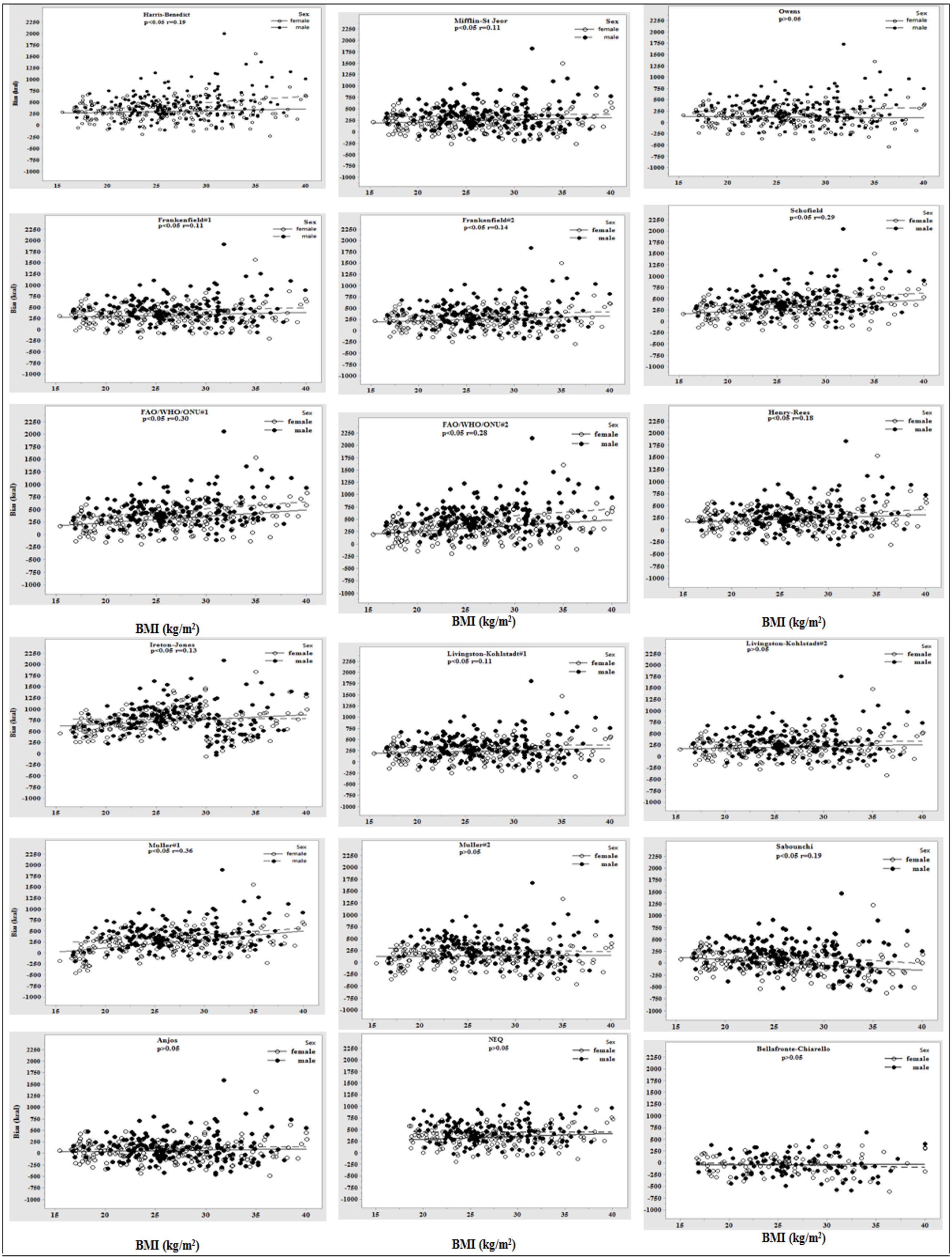

Figure 2. Scatter plots of the bias between REE determined by indirect calorimetry and by sixteen prediction equations against the mean of body mass index. Analysis performed with the total sample. Bias (kcal/d) for each REE prediction equation was determined by subtracting mREE from pREE. The gray solid line is the regression line for the measurement bias plotted against the body mass index for female and the gray dashed line for male subjects. Pearson correlation test was applied for measurement the correlation between bias and body mass index and its value is presented in the graphic. Separate plots are presented for each equation. The name of each equation ploted is in the graphic and is referee to as the same named presented in Table 1. For NEQ equation, underweight subjects were not evaluated as the equations developed are only for normal weight to obese subjects. For Bellafronte-Chiarello equation, the equation was evaluated using subjects form validation group (see Table 3)

In the total sample (Table 5), all REE predictive equations were biased: the lowest RMSE and the highest accuracy rates were from Anjos, Sabounchi, and Owens equations. For the underweight sample (Table 6), Muller#1 was the only equation unbiased at the group level: the lowest RMSE was from Anjos, Muller#1, and Sabounchi, and the highest accuracy rates from Anjos, Henry-Rees, and Owens. In the normal weight sample (Table 7), all REE predictive equations were biased: the lowest RMSE and the highest accuracy rates were from Anjos, Sabounchi, and Owens. In the overweight sample (Table 8), all REE predictive equations were biased, with the lowest RMSE and highest accuracy rates from Anjos and Sabounchi. In the obese sample (Table 9), Sabounchi was the only equation unbiased at the group level: the lowest RMSE were from Sabounchi and Anjos, and the highest accuracy rates from Anjos and Owens equations.

In almost all REE predictive equations evaluated, a decrease in RMSE was observed with an increase in BMI classification, except in the obese group. The exceptions were FAO/WHO/ONU#1, Ireton-Jones, and Muller#1 and #2: the RMSE did not present a pattern of behavior.

Schofield and FAO/WHO/ONU#1 and #2 equations maintained their accuracy rates without major changes regardless of increase in BMI classification and with the highest accuracy rate in the underweight subgroup. Harris-Benedict equation had a similar pattern, but the underweight subgroup had the lowest accuracy rate. For Ireton-Jones, the accuracy rate was always less than 10%. For Sabounchi and Anjos, the accuracy rate increased with increasing BMI classification and decreased in the obese group. For the other equations, there was a tendency to a higher accuracy rate as the classification of BMI increased.

Concerning underprediction rate, in general, the equations maintained the underestimation rate as BMI classification increased. For Owens, an increase in the underprediction rate was observed as BMI classification increased. For Muller#1 and #2, a considerable underprediction rate was observed in the underweight group, especially for Muller#1. For Sabounchi, the obese group had a high underprediction rate.

Almost all equations had a tendency to decrease the overestimation rate as BMI classification increased. Muller#1 and #2 began to decrease the overprediction rate from normal weight individuals. The Ireton-Jones and Harris-Benedict equations maintained the overestimation rate regardless of BMI classification. FAO/WHO/ONU#1 and #2 and Schofield increased the overprediction rate as BMI classification increased.

4. Discussion

There has been limited research concerning the accuracy of predictive models in estimating REE in young healthy adults, across BMI spectrum and in a population from Latin America. The results of this study showed large errors with commonly applied equations, leading to severely inaccurate recommendations.

In general, Sabounchi, Anjos, and Owens predictive equations presented the best performances. Unfortunately, none of the equations evaluated were able to accurately predict REE in more than 60% of the time, in the total sample or BMI subgroups. In addition, all equations tended to overestimate REE; underestimation usually occurred in a small sample (except for the underweight group). For almost all equations, bias increased with increasing BMI and Bland-Altman plots presented large limits of agreement with fixed and systematic errors: the equations tended to overestimate mREE values at lower means and to underestimate values at higher means. Thus, weight management still benefits from indirect calorimetry assessment.

The equations of Muller [13] were generated from a German database. The BMI-weight-specific Muller#1 equation for underweight was developed with older (32.0±12.2 years) and more underweight (BMI: 16.3±1.6kg/m²) subjects than our sample. Probably, for this reason it presented low accuracy rate and large underprediction in underweight subgroup being not recommended.

The equation of Anjos [16], developed from 529 Brazilian adults (20 to 80 years old), was the one with the best performances. The original sample used for Anjos equation, despite being older (female: mean age of 45 years; male: mean age of 43 years), had similar BMI (25 kg/m^2 for both sexes) and REE (female: 1137kcal; male: 1395kcal), justifying the high accuracy rates and low bias. In its validation study [29], the accuracy rates were 77.5 and 59.3% for women and men, respectively, much greater than our results. As the validation sample was more similar to the original sample than our data (34 and 32 years old; BMI: 23.8 and 24.6 kg/m^2; REE: 1155 and 1500 kcal, for women and men, respectively), the improved accuracy is explained.

REE was estimated using 1 of the 20 Sabounchi meta-regression equations [14], a weight and height-based equation applicable to white men and women aged from 18 to 57 years and with the highest r^2 (0.804) of this group, thus better fitting our study subjects as they were adults and the majority was white. The ethnicity fit promoted by the meta-regression [14] improved the performance of pREE as this equation presented the best accuracy rates for normal and overweight subjects. A study developed with older adults (38.2±14.9 years old) of both sexes from USA [30] showed an accuracy rate of about 70% from this equation. As the studies used in the meta-regression are mostly derived from USA and Europe population, improved performance is explained.

The NEQ equation [15] was developed from a Mexican sample. Both equations had low accuracy rates and high bias toward overestimation, probably because they were derived from an older, more obese and with higher REE subjects than our sample.

Owens equation [22,23] has a good performance, presenting the best accuracy rates in overweigh and obese subjects. Recently, a study [15] evaluated the performance of several REE predictive equations in a Mexican population and found an accuracy rate around 43 and 39% in overweight and obese individuals, respectively, for Owens equation, values close to our results. In turn, an Italian study [31] showed higher accuracy rates of 72, 66, and 55% in normal, overweight, and obese subjects, respectively. However, they were older (48 years), more obese (BMI: 34.3 kg/m^2; 67% of obese participants), and with a higher REE (1609 kcal), characteristics that were more similar to the original Owens sample.

Henry-Rees equation [26] was developed using the FAO/WHO/ONU equations database with the exclusion of Italian soldiers and the addition of subjects from tropical regions, with the intention of having a more representative ethnic diversity. Despite this, it still had bias towards overestimation with fixed and systematic errors.

The data from the Livingston-Kohlstadt equation [27] derived from the original Harris-Benedict [20] and Owens data [22,23] with 367 individuals added to the sample. These authors utilized an allometric model based on the relationship between REE and body size, supposing it would confer a better ability to predict REE in obese individuals. In our study, Livingston-Kohlstadt equation was better than Harris-Benedict but not than Owens equation in overweight and obese subjects. Two studies [28,31] observed that accuracy rate of Livingston-Kohlstadt equations decreased as BMI increased, and fall dramatically [28] within those with BMI>50 kg/m^2, showing that they are not appropriate for the morbidly obese.

The FAO/WHO/ONU #1 and #2 equations [8,9] had the worst performance, with bias toward overestimation in overweight and obese Mexicans [15]. In a study with Brazilian obese woman [32], FAO/WHO/ONU and Harris-Benedict had accuracy rates of 35 and 40%, higher than our results, but, as emphasized by the authors, Bland-Altman plots showed poor agreement, limiting their use in clinical practice for weight management.

Evidence analysis by the American Dietetic Association [6] has lent support to Mifflin-St Jeor equation [25] as the most appropriate for predicting REE in non-obese and obese subjects. A study with Brazilian subjects [29] showed a better performance for Mifflin-St Jeor equation between overweight to obese compared to leaner subjects, in agreement with our results once this equation increased accuracy rates as BMI classification increased. But, although the 2005 Evidence Working Group [6] recommended the use of Mifflin-St. Jeor equation for predicting REE, the results of our study and others [29,32] suggest that it is inappropriate for use in young Brazilian adults.

The Schofield equation [21], recommended for international use by the World Health Organization, resulted in overestimation of REE and low accuracy rates, as seen by others [16,29,32]. Therefore, although recommended by a respected international association, Schofield equation was found inappropriate for adults in Brazil.

The Frankenfield equations [28] tended to have lower RMSE with increasing BMI classification and its highest accuracy rate was observed among obese subjects. However, the high overprediction rates compromises the use of these equations in young adults, as observed by others [33].

The Harris-Benedict equation [20] is still widely used in clinical settings. However, its predictive capacity has been shown to be low with a tendency for overestimation, as seen by Anjos and colleagues [16], with accuracy rates around 20% when applied in Brazilian adults. The tendency for overprediction of REE was also observed by other studies [33]. Based on our findings, we do not recommend the use of Harris-Benedict equation for predicting REE among Brazilian adults.

The Ireton-Jones equation [24] presented the worst accuracy rates and performance, probably because it was developed from subjects before bariatric surgery with a much higher obesity degree than our participants.

Besides the use of REE predictive equations in their original form, the substitution of the current body weight for an adjusted one is a common practice for predicting REE even with worse accuracy rates [28] as a result. Clinicians also commonly apply a fixed REE of 25 or 30 kcal/kg/day or 2000 kcal for females and 2500 kcal for males: as can be seen in Table 2, regardless of sex and BMI classification, the mean mREE was always below 1600 kcal and the highest REE in women and in men was less than 2000 and 2500 kcal, respectively; in addition, mean mREE/weight was less than 20 kcal/kg/day. Therefore, the use of fixed values is not recommended.

The developed new predictive equation showed low bias and good performance from normal to obese subjects. Because the large limits of agreement seen by Bland-Altman plots, the equation needs to be extensively tested before a recommendation could be made.

This study has several strengths and limitations. As strengths, the REE was measured by indirect calorimetry, a reference method, with a validated system [18]; its reproducibility, evaluated in a subsample, was proved to be high. All measurements were done by the same trained and experienced dietitian at the same time, in standardized conditions for all groups and the adherence to the protocol was verified prior to measurements. The inclusion of subjects with BMI ranging from undernourished to obese allowed a more comprehensive analysis of REE predictive equations performance. Thus, the analyses performed can be generalized to individuals with diverse body composition.

Once not only one REE equation can be used for prediction of energy needs of subjects from different populations, it is necessary to evaluated the validation of REE prediction equations in different races, mainly in the marginally represented, as an example of Latin American populations. This is the first study to evaluate the predictive power of numerous REE equations, including three newer equations [14-16], in a large sample of Brazilians across BMI spectrum. Furthermore, the application of statistical tests detailing the accuracy at group and individual levels allowed a detailed analysis of pREE and the limitations of each predictive equation.

As limitations, the applicability of the results is restricted to adult individuals and cannot be extrapolated to children or elderly. Also, as Brazil is a multiethnic country, the low participation of African descendants in our sample is a negative point.

5. Conclusions

In conclusion, this study showed a wide variation in the accuracy of predictive equations when applied in healthy Brazilian adults. The new equation presented a good performance from normal weight to obese subjects but needs to be extensively tested before a recommendation could be made. The predictive equations with the best performance were Anjos among underweight, Anjos and Sabounchi among normal and overweight, and Anjos and Owens among obese. However, the poor accuracy rates highlight a caution application: until a more accurate formula is developed, the equations cited above may be recommended for estimating energy needs in Brazilian health adults respecting BMI subgroups as a starting point in nutritional therapy and the energy content may need to be later adjusted based on clinical signs and judgment. Indirect calorimetry is still necessary when the most accurate information about energy needs is needed.

Taking all these findings into account, the development of low cost and portable indirect calorimetry equipment, as well as the extensive validation of these new devices in comparation with a reference method, are a broad field of research, once REE prediction equations still lack desired accuracy.

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Statement of Competing Interests

The authors have no competing interests.

List of Abbreviations

BMI: body mass index; FFM: fat free mass; FFMI: fat free mass index; FM: fat mass; FMI: fat mass index; mREE: measured REE by indirect calorimetry; pREE: predicted REE by prediction equations; REE: resting energy expenditure; RMSE: root mean square error; SEE: standard error of the estimate.

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Transparency Declaration

The lead author affirms that this manuscript is an honest, accurate and transparent account of the study. No important aspects of the study were omitted and any discrepancies from the study as planned was explained. The reporting of this work is compliant with STROBE guideline.

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