Cross-Validation of Resting Metabolic Rate Prediction Equations

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Running head: RMR prediction accuracy

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List of abbreviations:

RMR: Resting metabolic rate

FFM: Fat-Free mass

FM: Fat mass

feCO2: Fraction of End Tidal CO2 (fraction of expired CO2)

VCO2: Rate of Elimination of Carbon Dioxide

VO2: Oxygen uptake/ consumption

DXA: Dual-energy X-ray absorptiometry

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Abstract

Background: Resting metabolic rate (RMR) measurement is time consuming and requires specialized equipment. Prediction equations provide an easy method to estimate RMR; however, their accuracy likely varies across individuals. Understanding the factors that influence the accuracy of RMR predictions will help to revise existing or develop new and improved equations.

Objective: To test the validity of RMR predicted in healthy adults by the Harris-Benedict, WHO, Mifflin-St.Jeor, Nelson, Wang equations and three meta-equations of Sabounchi.

Design: Predicted RMR was tested for agreement with indirect calorimetry.

Participants/setting: Men and women (n=30) age 18-65y from Grand Forks, ND were recruited and included for analysis during Spring/Summer 2014. Participants were nonobese or obese (BMI range 19-39 kg/m^2) and primarly Caucasian.

Main outcome measure: Agreement between measured (indirect calorimetry) and predicted RMR.

Statistical analysis: The methods of Bland and Altman were employed to determine mean bias (predicted minus measured RMR, kcal/day) and limits of agreement between predicted and measured RMR. Repeated measures ANOVA was used to test for bias in RMR predicted from each equation versus the measured RMR.

Results: Bias (mean ± 2 SD) was lowest for the Harris-Benedict (-14 ± 378 kcal/24 hrs) and WHO (-25 ± 394 kcal/24 hrs) equations. These equations also predicted RMR that were not different from measured. Mean RMR predictions from all other equations significantly differed from indirect calorimetry. The 2 SD limits of agreement were moderate or large for all equations

tested ranging from 314 to 445 kcal/24 hrs. Prediction bias was inversely associated with the magnitude of RMR and with FFM.

Conclusions: At the group-level, the traditional Harris-Benedict and WHO equations were the most accurate. However, these equations did not perform well at the individual-level. As FFM increased, the prediction equations further underestimated RMR.

Introduction

An individual's resting metabolic rate (RMR) is defined as the energy required for vital body functions at rest and is the largest contributor to daily total energy expenditure.[1] Accurate measurement of RMR is important in scientific and clinical settings when determining daily energy needs.[2] Computerization and technological advances in the quantitation of flow rate and gas concentration has given rise to metabolic carts that are widely used to measure RMR. However, indirect calorimetry is expensive and time consuming, which limits its practicality in field and clinical settings. Moreover, accurate measurement of RMR requires much control before and during the testing as many factors such as food intake, some drugs, physical activity, room temperature, and time of day can all influence RMR.[3] For these reasons, prediction equations based on body weight, height, sex, and other individual differences have been developed, with an early example being the work of Harris and Benedict.[4] Resting metabolic rate prediction equations are usually developed and validated using data collected from individuals of a wide range of age, race, sex, body composition and other physical characteristics. As such, RMR prediction equations may not be accurate when applied at the indvidual level if that individual differs in one or more characteristics from the original population used to develop and validate the equation.

One physical characteristic that may affect RMR prediction accuracy is fat-free mass (FFM). Fat-free mass has a greater metabolic rate than fat mass (FM) and as such is a predominate determinant of RMR, explaining 53% to 88% of the variance in RMR.[5, 6] The strong association of FFM with RMR has spurred investigators to develop prediction equations that include FFM as a predictor variable.[6-17] Wang and colleagues[18] recently concluded that the RMR-FFM relationship has a curvilinear function, as a linear relationship results in a positive

intercept that can vary from 186 to 662 kcal/d.[18] In efforts to increase the accuracy of RMR predictions from FFM, Wang developed an equation based on the finding that the relationship between RMR and FFM is linear only within the 40-80 kg FFM interval, the range of most humans.[18] Nelson and colleagues also used FFM to predict RMR, but added FM as a predictor, arguing that the addition increased accuracy of the equation.[5] Sabounchi and colleagues[1] took another approach to improve RMR prediction by developing population-specific meta-regression equations derived from 47 previously published RMR prediction equations.[1] The resulting equation 'structures' are proposed to provide a more targeted prediction equation based on the population characteristics being studied.

The equations of Sabounchi,[1] have not yet been been cross-validated in healthy adults and there are few data on whether the predicted RMR from the Wang,[18] or Nelson[5] equations differ from those of the Mifflin-St.Jeor,[17] Harris-Benedict,[4] and WHO[19] equations. The Mifflin-St.Jeor,[17] Harris-Benedict,[4] and WHO[19] equations have been cross-validated in both healthy and hospitalized patients though the conclusions regarding their accuracy have differed across studies.[20-26] Thus, the purpose of the present work was to test differences in the prediction bias of these eight equations that were developed using varying conceptual strategies, in a group of healthy adults. An additonal aim was to determine, for each equation, the association of the magnitude of prediction bias with the magnitude of FFM and FM.

Materials and Methods

Participants

A total of 30 adults (15 men) participated in the study. Recruitment occurred during the spring and summer of 2014 in the greater Grand Forks, North Dakota metropolitan area. Participants were a sample who responded to recruitment media including printed brochures and fliers and online advertisements on the Grand Forks Human Nutrition Center Website. The intention was to recruit an equal number of men and women. Participants were reimbursed $200 for their participation. Entry criteria included no known diseases affecting metabolic rate, not taking medications that affect energy expenditure, and not using tobacco. Pregnant and/or lactating women were not allowed to enroll. Women were measured in the same phase of their menstrual cycle at two study visits, as these visits were within two days and no woman had reported beginning a new menstrual cycle on the second visit. The study was powered based on the width of the confidence interval around the mean prediction error. Twenty-nine participants were needed to have 90% power to obtain a 95% confidence interval of +/- 100 kcal, assuming a standard deviation of 225 kcal.[20] The study was approved by the University of North Dakota Institutional Review Board and all participants provided written informed consent prior to participating in the study.

Design

Each participant completed two RMR sessions on nonconsecutive days (Monday and Wednesday, Tuesday and Thursday, or Wednesday and Friday of the same week). Participants drove by automobile to the laboratory in the morning after not exercising, consuming food or caffeine for 12 hours or alcohol for 24 hours. Participants completed an Eating and Exercise History questionnaire to ensure that they had adhered to study testing instructions. All

participants reported adhering to the instructions. All participants completed a single dual-energy x-ray absorptiometry (DXA) scan for assessment of body composition.

Measurements

Height and weight***:*** Height was measured in triplicate to the nearest 0.1 cm using a stadiometer (Seca; Chino, CA). Body weight was measured using a calibrated digital scale (Tanita BC-418; Tokyo) to the nearest 0.1 kg on each visit. Height and weight from visit one were used to calculate RMR from the prediction equations. Participants were measured wearing either provided lab scrubs or light casual clothes (t-shirt, shorts) and not wearing shoes. No adjustment for this minimal clothing was included in the measurement of body weight.

Resting metabolic rate: Resting metabolic rate was measured using indirect calorimetry (TrueOne, 2400; Parvo Medics, Sandy, UT) with a ventilated canopy. The TrueOne 2400 is a mixing chamber system that uses a paramagnetic oxygen analyzer (range 0–25%) and an infrared, single beam, single wave-length carbon dioxide analyzer (range 0–10%). Before each test, calibrations were performed on the flow meter using a 3.0-L syringe and on the gas analyzers using verified gases of known concentrations. After 30 minutes of quiet rest in the supine position in a dimly lit, temperature-controlled room between 22 and 24 C, RMR was measured for 30 minutes. The test was monitored to ensure participants remained awake and between 0.8 and 1.2% $feCO_2$. Criteria for a valid RMR was a minimum of 15 min of steady state, determined as a <10% fluctuation in oxygen consumption and <5% fluctuation in respiratory quotient. The Weir equation[27] was used to determine RMR from the measured

oxygen consumption and CO_2 production. The ParvoMedics TruOne 2400 metabolic cart is reliable with across-day Pearson correlation coefficients of 0.994 and 0.991 for VO_2 and VCO_2, respectively, and coefficients of variation (CV) for VO_2 and VCO_2 of 4.7 and 5.7%, respectively.[28] The mean RMR value of the two tests for each participant was used as the measured indirect calorimetry value. The within participant CV for 24-hour RMR was 5.6% between these two tests.

Dual-energy x-ray absorptiometry: Body composition was determined using dual energy x-ray absorptiometry (GE Lunar iDXA, software version 14.10.022). The iDXA technique allows the non-invasive assessment of soft tissue composition by region with a precision of 1-3%.[29] These data were used to obtain whole body lean mass, fat mass, bone mineral content, and bone mineral density. Total FFM was calculated as lean mass + bone mineral content. Calibration to external standards was performed prior to actual data collection.

Prediction equations: Table 1 summarizes the eight prediction equations cross-validated in the present study. In addition to the Harris-Benedict,[4] Mifflin-St.Jeor,[17] WHO[19] equations, the equation structures 4, 5 and 11 of Sabounchi[1] were included as these three structures produced the greatest R^2 for individuals of the same age and ethnicity recruited for the current study. Equation 11 of Wang[18] and the Nelson equation[5] were included because of their use of the relationship of RMR with FFM and RMR with FFM and FM, respectively.

Statistical Analysis

Repeated measures ANOVA was used to test for differences in mean RMR (kcal/day) obtained from the metabolic cart and the eight prediction equations. Post-hoc comparisons between RMR from each prediction equation and the metabolic cart were made using Dunnett's test. Agreement between indirect calorimetry measured RMR and predicted RMR was analyzed by the Bland and Altman method.[30] Differences in predicted and measured RMR were calculated for each participant both as the bias in kcal/24 hr (predicted RMR minus indirect calorimetry RMR measurement) and as the percentage difference between the predicted RMR and indirect calorimetry values. An accurate predicted value was defined as one that fell within +/- 10% of the value obtained from the metabolic cart while over predictions were considered to be $\geq$10% and under predictions were $\leq$-10%.[20, 21, 31] Separate linear regression analyses were performed between the prediction bias (kcal/24 hr) and total FFM and FM. An alpha level was set at 0.05 to indicate statistical significance.

Results

There were no significant differences between men and women for participant characteristics (Table 2). Figure 1 shows the Bland and Altman plot results for the eight prediction equations. The mean bias, the 95% limits of agreement ($\pm$ 2 SD), as well as the regression line, are shown in each plot. A positive value indicates the predicted RMR was greater than the measured RMR. The bias in RMR ranged from -14 to -190 kcal/24 hrs. At the individual-level, the 95% limits of agreement were great for all of the equations tested ranging from -620 to +370 kcal/24 hrs. All equations tested had individual bias values near or exceeding the $\pm$ 2 SD limits of agreement. For all equations there was a significant inverse relationship between prediction bias and RMR. At the group-level, ANOVA (Table 3) indicated that the

Harris-Benedict and WHO predictions did not differ from the indirect calorimetry measured RMR. All other equations under-predicted ($p<0.001$) RMR compared to indirect calorimetry.

Table 3 also provides a summary of the bias expressed as the percentage difference in predicted RMR. This analysis accounts for individual differences in RMR and suggests that, at the group-level, the Harris-Benedict, WHO, and Sabounchi's structure 4 were the most accurate equations, predicting RMR within 1% to 2.5% of the metabolic cart-determined value. As shown in Table 4, at the group-level, the Harris-Benedict equation provided accurate RMR predictions in 23 of 30 participants, and over- and under-predicted RMR in 4 and 3 of 30 participants, respectively. In contrast, the Nelson equation provided accurate RMR predictions in only 16 of 30 participants with no over-predictions.

Figure 2 demonstrates that all but the Nelson equation produced an inverse relationship between prediction bias and magnitude of FFM. As shown in Figure 3, prediction bias was not associated with the amount of FM. There were no differences in the relationship between prediction bias and FFM when the male and female data were analyzed separately and the relationship between bias and fat mass was not different between males and females.

Discussion

The present study evaluated the accuracy of RMR prediction equations in a sample of healthy adults. Conclusions regarding accuracy of the prediction equations depended on whether accuracy was being assessed at the group- or individual-level. The current work demonstrates that the Harris-Benedict, Mifflin-St. Jeor and WHO equations, based on weight, sex and age, had greater accuracy (percent of predicted RMR within ±10% of measured RMR). Though the Mifflin-St. Jeor equation was second to the Harris-Benedict equation for percentage of

accurately predicted RMR, it under predicted RMR (Table 3) despite being proposed as an improvement over the Harris-Benedict equation at the time of its development.[17] In individuals of similar age and health status, the Harris-Benedict equation has historically accurately predicted RMR in 38% to 80% of individuals,[31] while the Mifflin-St. Jeor equation accurately predicted RMR in 70% to 82% of individuals.[21, 26] The current results also agree with others reporting the accuracy of the Harris-Benedict, Mifflin-St. Jeor, and WHO equations to be 70%, 79%, and 67% of individuals, respectively.[20] In addition, at the group-level, only the Harris-Benedict and WHO equations had mean predicted RMR that did not differ from measured RMR (Table 3) and the inaccurately predicted RMR values were nearly evenly distributed as over- and under-predictions (Table 4). The Bland Altman analyses provide unique insights into the performance of the equations in that they demonstrate that, due to wide limits of agreement (Table 3, Figure 1), even the Harris-Benedict and WHO equations did not perform well at the individual-level. This was especially evident in individuals with greater RMR and FFM in that under-prediction bias increased as RMR or FFM increased (Figures 1 and 2).

The robust relationship between FFM and RMR has led some investigators to develop RMR prediction equations based on FFM. Indeed, the recently derived meta-regression Structures 4, 5, and 11 from Sabounchi,[1] and the equations of Wang[18] and of Nelson[5] utilize either FFM or both FFM and FM to estimate RMR. Sabounchi structure 4[1] had a high accuracy rate of 73.3% (Table 4), but the other structures tested under predicted RMR (Table 3). Both the Wang[18] and Nelson[5] equations reduced the relationship between RMR prediction bias and FFM (Figure 2), these equations also had the greatest underprediction bias of RMR (Table 3). Individual-level data show (Figure 1) that this was due to the distribution of the predicted values, as nearly all of the inaccurate estimations by these equations were under predictions.

Thus, the utility of RMR prediction equations based on FFM can be questioned given the additional time, expertise and expense that is required to measure FFM using accurate methods such as dual x-ray absorptiometry or hydrodensitometry. Sabounchi[1] demonstrated that weight can provide nearly the same predictive ability of RMR as FFM, and that age and including a greater constant term account for a significant portion of FFM contribution to RMR. Even with the accurate FFM measures used in the present study, the equation of Wang[18] and that of Nelson[5] did not have high accuracy. However, there is promising evidence from the work of Sabounchi,[1] who combined the results from multiple studies to develop meta-regressions, that continued refinement of such equations could result in a greater rate of accurate RMR predictions.

To account for individual differences in RMR, bias was also calculated as a percentage of measured RMR (Table 3). Estimates from the Harris-Benedict and WHO equations, and from structure 4 of Sabounchi were not different from indirect calorimetry. These same results are reflected in the Bland Altman plots (Figure 1), indicating predictions well within the limits of agreement for these equations at RMR values under 2000 kcal. In agreement with previous work,[5, 18, 32-34] the regression analyses (Figure 2) provide evidence that the inverse relationship between prediction bias and RMR is likely a function of greater FFM. Fat-free mass consists of multiple organs and tissues with different metabolic rates, and as such, the RMR/FFM ratio decreases with increasing FFM.[12, 18, 35] The brain, liver, heart, and kidneys account for 60–70% of RMR in adults, whereas their combined weight is less than 6% of total body weight. Skeletal muscle, on the other hand, comprises 40–50% of total body weight and accounts for 20–30% of RMR.[33, 34, 36] With increasing muscle mass the more metabolically active organs occupy a decreasing fraction of FFM so that, in individuals with greater muscle mass and thus FFM, the

organs with greater metabolic rates will contribute a smaller proportion of the total RMR. Although including organ masses in a RMR prediction equation brings the y-intercept to zero,[33] the inclusion of organ masses in stepwise regression does not improve the prediction of RMR over a more traditional model using only FFM.[37] Others have confirmed that RMR is influenced not by organ mass, but by the energy expenditure per kilogram of the organ.[34, 37] The internal organs have a greater RMR/kg than skeletal muscle, therefore the proportional contribution of the internal organs to total RMR decreases with increasing FFM[12, 18, 34-38] may help to explain why these prediction equations underestimate RMR. The differing proportional contributions of the internal organs to total RMR may not be well modeled in current FFM-based RMR prediction equations. In contrast, others have concluded that the relative contribution of the liver, heart, and kidneys to RMR is consistent across a wide range of FFM.[39, 40] The brain is one of the most metabolically active organs consuming about one-fifth of total body oxygen.[39] The metabolic rate of the brain; however, is negatively correlated with FFM,[39] potentially identifying another source of variability RMR prediction equations do not model.

Strengths of the present study include accurate measures of FFM to allow for testing of the association of individual differences in FFM with the bias between measured and predicted RMR. Use of the average of RMR tests conducted on two days and using the previously validated TrueOne, 2400 metabolic cart[28] are additional strengths. However, this study is not without limitations. The lack of ethnic diversity of the participants limits the generalizability of the results. Though the power calculations suggested that the sample size was adequate to test the primary analysis, the sample size did not allow for testing differences in prediction equation accuracy between men and women or the effect of BMI on accuracy. Future studies may benefit from focusing on particular populations such as obese participants, a specific sex, or a particular

ethnic group. This will allow adequate power in determining the cross-validity of RMR predictions among sub-populations.

Conclusions

The present study demonstrates that at the group-level the Harris-Benedict and WHO equations estimate RMR with a bias of <1% and that the predicted RMR from these equations fell within ±10% of the value obtained from indirect calorimetry for 23 of 30 and 20 of 30 participants. However, the Bland Altman analyses revealed wide 2 SD limits of agreement for all equations at the individual-level. Thus, predicted RMR data should be used with caution when used to determine the daily energy needs of an individual in clinical or scientific settings. All of the tested equations became less accurate with increasing FFM. The present study supports the notion that individual differences in the amount of FFM contributes to between individual variability in RMR and RMR prediction accuracy.[12, 18, 34-38] The reduction in RMR prediction accuracy with greater amounts of FFM is likely due to the smaller proportional contribution of the internal organs to total RMR, and those equations developed from the FFM-RMR relationship may be most susceptible to such bias. Future studies are needed to determine other factors that might influence the RMR-FFM relationship, most notably, brain and organ metabolic rates. Until existing equations are refined or new equations are developed, the application of predicting RMR in research and clinical practice should continue to be undertaken with caution.

References

1. Sabounchi NS, Rahmandad H, Ammerman A. Best-fitting prediction equations for basal metabolic rate: informing obesity interventions in diverse populations. *Int J Obes (Lond)* 2013; 37: 1364-1370.

2. Abdel-Hamid TK. Modeling the dynamics of human energy regulation and its implications for obesity treatment. *System Dynamics Review* 2002; 18: 431-471.

3. Compher C, Frankenfield D, Keim N, Roth-Yousey L. Evidence Analysis Working G. Best practice methods to apply to measurement of resting metabolic rate in adults: a systematic review. *J Am Diet Assoc* 2006; 106: 881-903.

4. Harris JA, Benedict FG. A Biometric Study of Human Basal Metabolism. *Proc Natl Acad Sci U S A* 1918; 4: 370-373.

5. Nelson KM, Weinsier RL, Long CL, Schutz Y. Prediction of resting energy expenditure from fat-free mass and fat mass. *Am J Clin Nutr* 1992; 56: 848-856.

6. Cunningham JJ. A reanalysis of the factors influencing basal metabolic rate in normal adults. *Am J Clin Nutr* 1980; 33: 2372-2374.

7. Owen OE, Kavle E, et al. A reappraisal of caloric requirements in healthy women. *Am J Clin Nutr* 1986; 44: 1-19.

8. Luke A, Schoeller DA. Basal metabolic rate, fat-free mass, and body cell mass during energy restriction. *Metabolism* 1992; 41: 450-456.

9. Ravussin E, Burnand B, Schutz Y, Jequier E. Twenty-four-hour energy expenditure and resting metabolic rate in obese, moderately obese, and control subjects. *Am J Clin Nutr* 1982; 35: 566-573.

10. Ravussin E, Lillioja S, Anderson TE, Christin L, Bogardus C. Determinants of 24-hour energy expenditure in man. Methods and results using a respiratory chamber. *J Clin Invest* 1986; 78: 1568-1578.

11. McNeill G, Rivers JP, Payne PR, de Britto JJ, Abel R. Basal metabolic rate of Indian men: no evidence of metabolic adaptation to a low plane of nutrition. *Hum Nutr Clin Nutr* 1987; 41: 473-483.

12. Ravussin E, Bogardus C. Relationship of genetics, age, and physical fitness to daily energy expenditure and fuel utilization. *Am J Clin Nutr* 1989; 49: 968-975.

13. Owen OE, Holup JL, et al. A reappraisal of the caloric requirements of men. *Am J Clin Nutr* 1987; 46: 875-885.

14. Owen OE. Resting metabolic requirements of men and women. *Mayo Clin Proc* 1988; 63: 503-510.

15. Heshka S, Yang MU, Wang J, Burt P, Pi-Sunyer FX. Weight loss and change in resting metabolic rate. *Am J Clin Nutr* 1990; 52: 981-986.

16. Kashiwazaki H, Suzuki T, Inaoka T. Postprandial resting metabolic rate and body composition in the moderately obese and normal-weight adult subjects at sitting posture. *J Nutr Sci Vitaminol (Tokyo)* 1988; 34: 399-411.

17. Mifflin MD, St Jeor ST, et al. A new predictive equation for resting energy expenditure in healthy individuals. *Am J Clin Nutr* 1990; 51: 241-247.

18. Wang Z, Heshka S, et al. Resting energy expenditure-fat-free mass relationship: new insights provided by body composition modeling. *Am J Physiol Endocrinol Metab* 2000; 279: E539-545.

19. Energy and protein requirements. Report of a joint FAO/WHO/UNU Expert Consultation. *World Health Organ Tech Rep Ser* 1985; 724: 1-206.

20. Weijs PJ. Validity of predictive equations for resting energy expenditure in US and Dutch overweight and obese class I and II adults aged 18-65 y. *Am J Clin Nutr* 2008; 88: 959-970.

21. Frankenfield DC, Rowe WA, Smith JS, Cooney RN. Validation of several established equations for resting metabolic rate in obese and nonobese people (vol 103, pg 1152, 2003). *J Am Diet Assoc* 2003; 103: 1593-1593.

22. Hasson RE, Howe CA, Jones BL, Freedson PS. Accuracy of four resting metabolic rate prediction equations: effects of sex, body mass index, age, and race/ethnicity. *J Sci Med Sport* 2011; 14: 344-351.

23. Schusdziarra V, Wolfschlager K, Hausmann M, Wagenpfeil S, Erdmann J. Accuracy of resting energy expenditure calculations in unselected overweight and obese patients. *Ann Nutr Metab* 2014; 65: 299-309.

24. Miller S, Milliron BJ, Woolf K. Common Prediction Equations Overestimate Measured Resting Metabolic Rate in Young Hispanic Women. *Top Clin Nutr* 2013; 28: 120-135.

25. Kim do K. Accuracy of predicted resting metabolic rate and relationship between resting metabolic rate and cardiorespiratory fitness in obese men. *J Exerc Nutrition Biochem* 2014; 18: 25-30.

26. Frankenfield DC. Bias and accuracy of resting metabolic rate equations in non-obese and obese adults. *Clin Nutr* 2013; 32: 976-982.

27. Weir JBD. New Methods for Calculating Metabolic Rate with Special Reference to Protein Metabolism. *Journal of Physiology-London* 1949; 109: 1-9.

28. Crouter SE, Antczak A, Hudak JR, DellaValle DM, Haas JD. Accuracy and reliability of the ParvoMedics TrueOne 2400 and MedGraphics VO2000 metabolic systems. *Eur J Appl Physiol* 2006; 98: 139-151.

29. Rothney MP, Martin FP, et al. Precision of GE Lunar iDXA for the measurement of total and regional body composition in nonobese adults. *J Clin Densitom* 2012; 15: 399-404.

30. Bland JM, Altman DG. Statistical methods for assessing agreement between two methods of clinical measurement. *Lancet* 1986; 1: 307-310.

31. Frankenfield D, Roth-Yousey L, Compher C. Comparison of predictive equations for resting metabolic rate in healthy nonobese and obese adults: a systematic review. *J Am Diet Assoc* 2005; 105: 775-789.

32. Bosy-Westphal A, Braun W, Schautz B, Muller MJ. Issues in characterizing resting energy expenditure in obesity and after weight loss. *Front Physiol* 2013; 4: 47.

33. Gallagher D, Albu J, et al. Small organs with a high metabolic rate explain lower resting energy expenditure in African American than in white adults. *Am J Clin Nutr* 2006; 83: 1062-1067.

34. Javed F, He Q, et al. Brain and high metabolic rate organ mass: contributions to resting energy expenditure beyond fat-free mass. *Am J Clin Nutr* 2010; 91: 907-912.

35. Heymsfield SB, Gallagher D, et al. Body-size dependence of resting energy expenditure can be attributed to nonenergetic homogeneity of fat-free mass. *Am J Physiol Endocrinol Metab* 2002; 282: E132-138.

36. Gallagher D, Belmonte D, et al. Organ-tissue mass measurement allows modeling of REE and metabolically active tissue mass. *Am J Physiol* 1998; 275: E249-258.

37. Sparti A, DeLany JP, delaBretonne JA, Sander GE, Bray GA. Relationship between resting metabolic rate and the composition of the fat-free mass. *Metab Clin Exp* 1997; 46: 1225-1230.

38. Couture P, Hulbert AJ. Relationship between body mass, tissue metabolic rate, and sodium pump activity in mammalian liver and kidney. *Am J Physiol* 1995; 268: R641-650.

39. Oshima S, Miyauchi S, et al. Relative Contribution of Organs Other Than Brain to Resting Energy Expenditure Is Consistent among Male Power Athletes. *J Nutr Sci Vitaminol (Tokyo)* 2013; 59: 224-231.

40. Oshima S, Miyauchi S, et al. Fat-free mass can be utilized to assess resting energy expenditure for male athletes of different body size. *J Nutr Sci Vitaminol (Tokyo)* 2011; 57: 394-400.

Figure Legends

Figure 1. Plots of the bias between resting metabolic rate (RMR) determined by indirect calorimetry and by eight prediction equations against the mean of the two methods for 30 adults age 19-64 years. Bias (kcal/day) for each of the eight equations predicting RMR was determined by subtracting equation predicted RMR from the metabolic cart measured (indirect calorimetry) RMR. The dashed line represents the mean measurement difference (predicted RMR– measured RMR) and the dotted lines correspond to the 95% limits of agreement (± 2 SD). The solid line is the regression line for the measurement bias plotted against the mean of the two methods.

Figure 2. Linear regression plots of the bias between resting metabolic rate (RMR) determined by indirect calorimetry against fat-free mass for 30 adults age 19-64 years. Bias (kcal/day) for each of the eight equations predicting RMR was determined by subtracting equation predicted RMR from the metabolic cart measured (indirect calorimetry) RMR. Separate plots are presented for each equation. Plots labelled 'Sabounchi structures' are population-specific meta-regression equations developed by Sabounchi et al.[1]

Figure 3. Linear regression plots of the bias between resting metabolic rate (RMR) determined by indirect calorimetry against fat mass for 30 adults age 19-64 years. Bias (kcal/day) for each of the eight equations predicting RMR was determined by subtracting equation predicted RMR from the metabolic cart measured (indirect calorimetry) RMR. Separate plots are presented for each equation. Plots labelled 'Sabounchi structures' are population-specific meta-regression equations or 'structures' developed by Sabounchi et al.[1]

Figure 1.

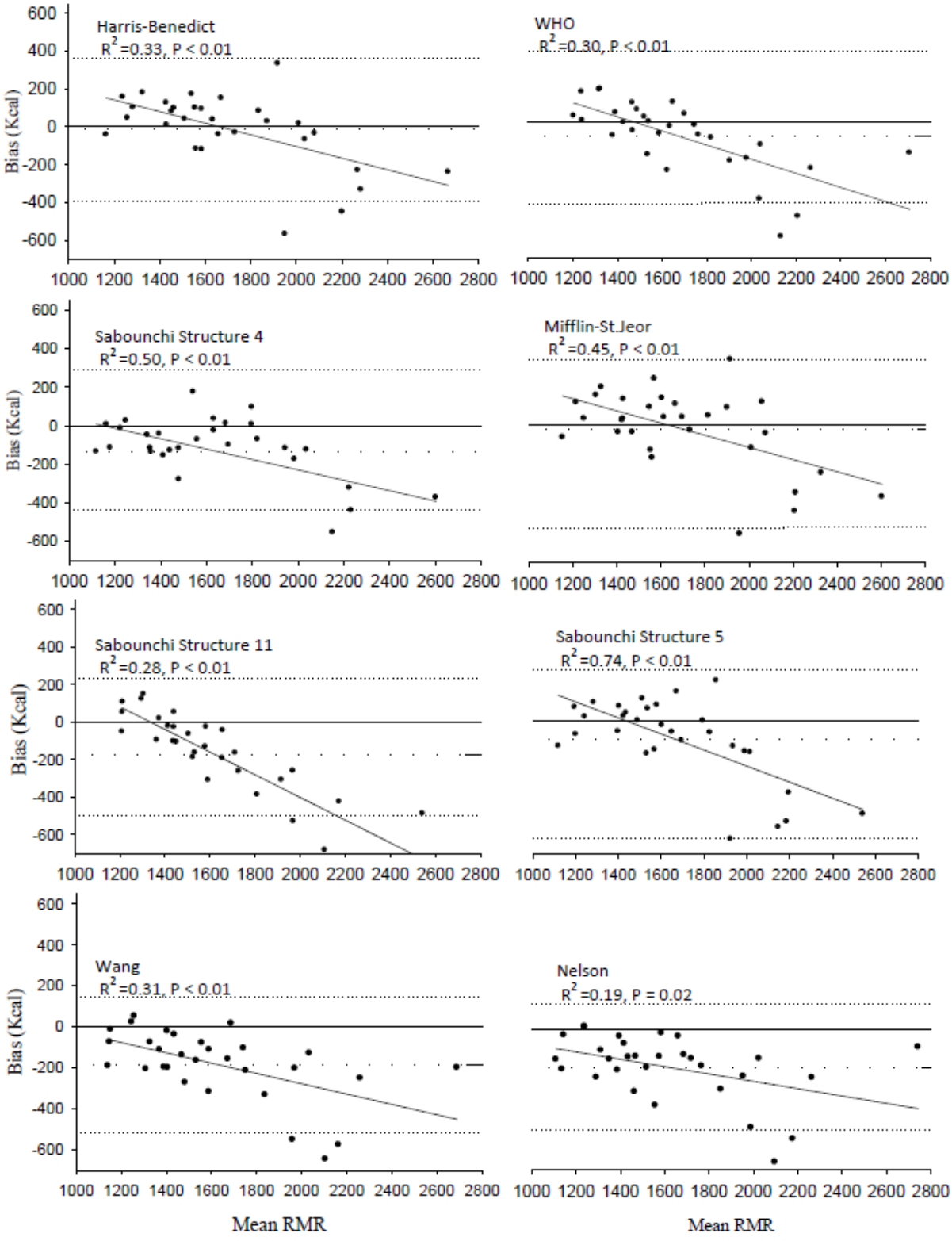
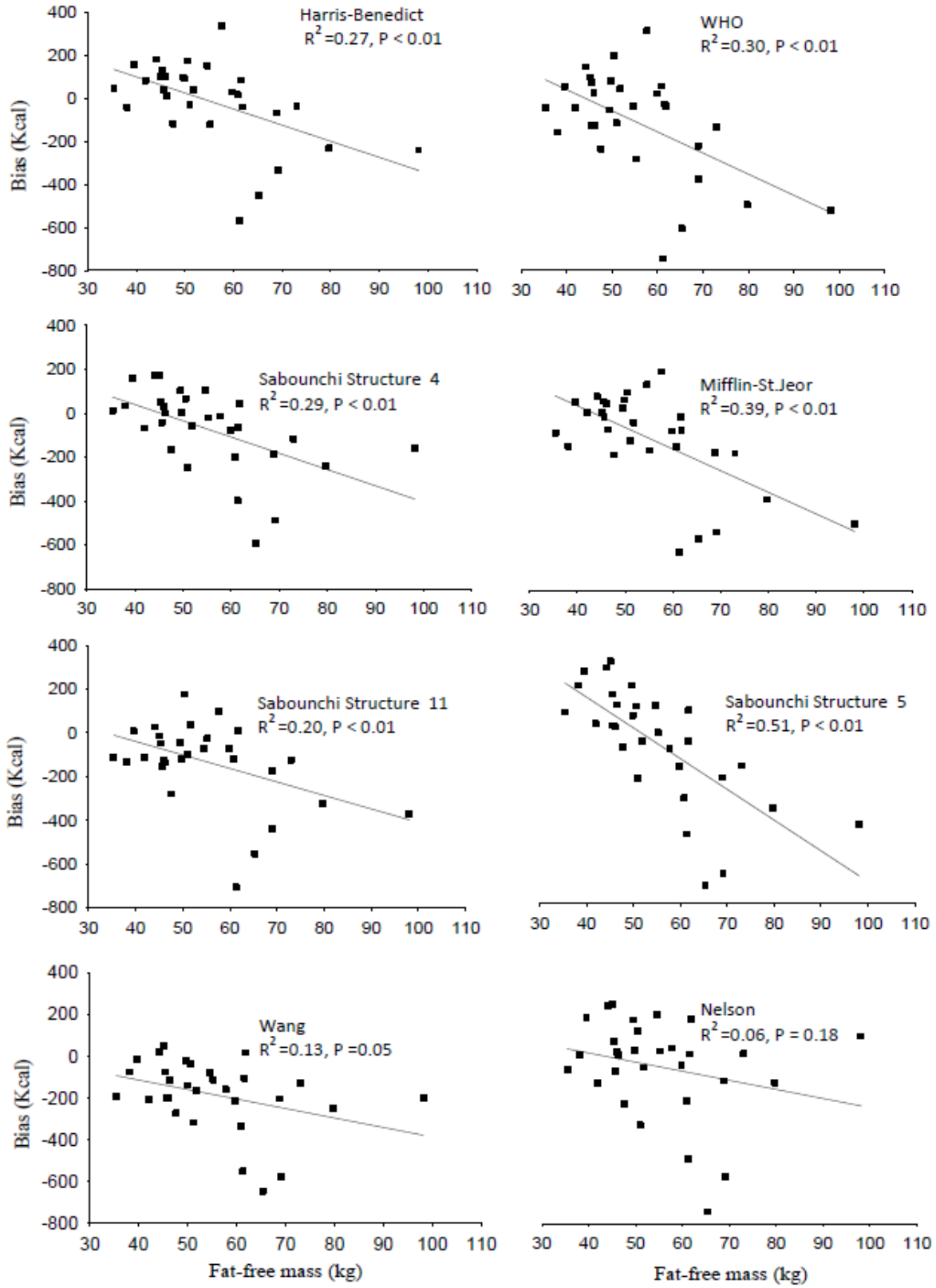
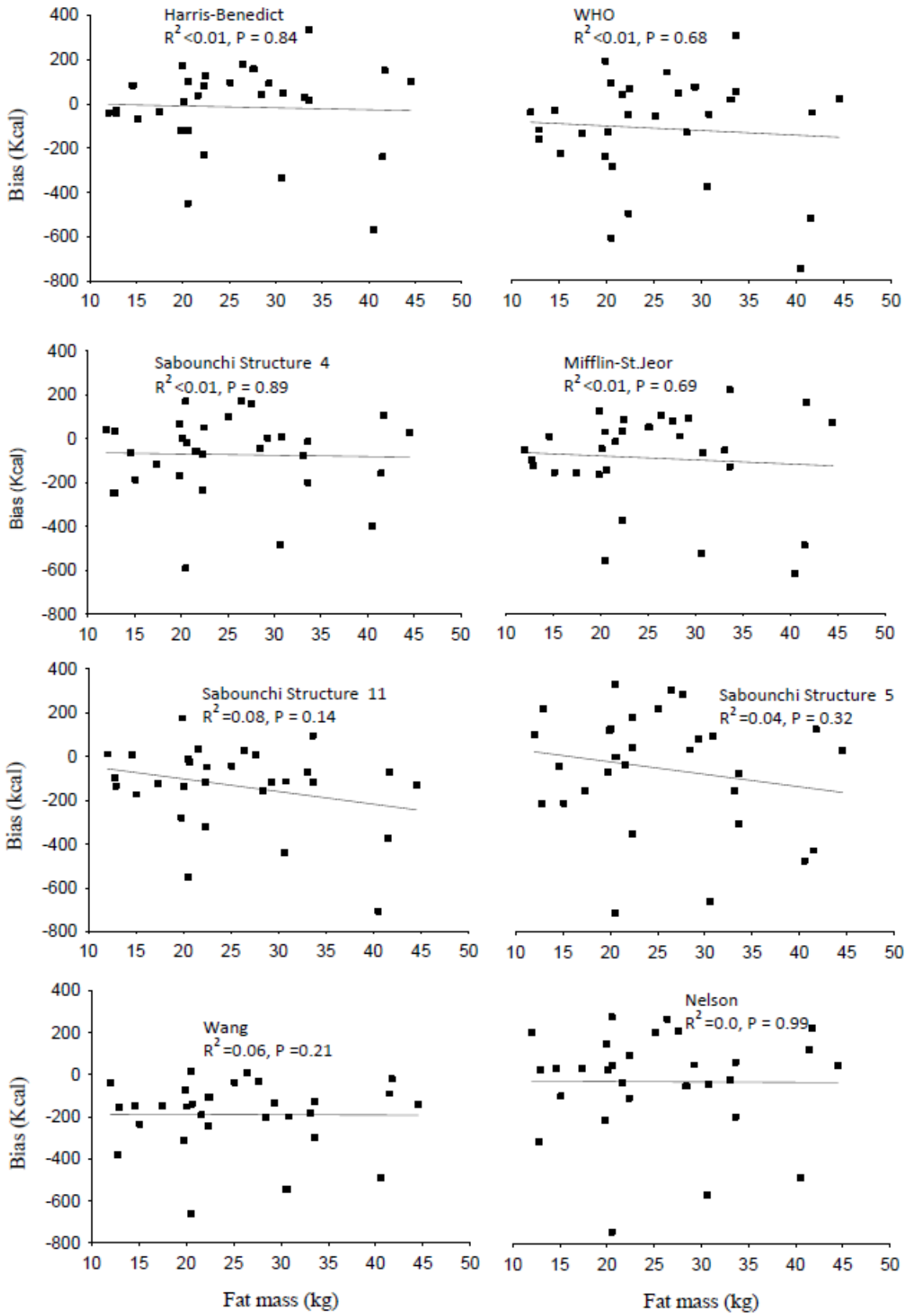

Harris-Benedict
R2=0.33, P < 0.01
WHO
R2=0.30, P < 0.01
Sabounchi Structure 4
R2=0.50, P < 0.01
Mifflin-St.Jeor
R2=0.45, P < 0.01
Sabounchi Structure 11
R2=0.28, P < 0.01
Sabounchi Structure 5
R2=0.74, P < 0.01
Wang
R2=0.31, P < 0.01
Nelson
R2=0.19, P = 0.02
Bias (Kcal)
Mean RMR
600
400
200
0
-200
-400
-600
1000 1200 1400 1600 1800 2000 2200 2400 2600 2800

Figure 2:


Harris-Benedict
R2=0.27, P < 0.01
WHO
R2=0.30, P < 0.01
Sabounchi Structure 4
R2=0.29, P < 0.01
Mifflin-St.Jeor
R2=0.39, P < 0.01
Sabounchi Structure 11
R2=0.20, P < 0.01
Sabounchi Structure 5
R2=0.51, P < 0.01
Wang
R2=0.13, P =0.05
Nelson
R2=0.06, P = 0.18
Bias (Kcal)
Fat-free mass (kg)
400
200
0
-200
-400
-600
-800
30
40
50
60
70
80
90
100
110

403

Figure 3:


Harris-Benedict
R2 <0.01, P = 0.84
WHO
R2 <0.01, P = 0.68
Sabounchi Structure 4
R2 <0.01, P = 0.89
Mifflin-St.Jeor
R2 <0.01, P = 0.69
Sabounchi Structure 11
R2 =0.08, P = 0.14
Sabounchi Structure 5
R2 =0.04, P = 0.32
Wang
R2 =0.06, P =0.21
Nelson
R2 =0.0, P = 0.99
Bias (Kcal)
Bias (kcal)
Fat mass (kg)
400
200
0
-200
-400
-600
-800
10
15
20
25
30
35
40
45
50

404

Table 1. Eight resting metabolic rate (RMR) prediction equations tested in the present study for agreement with indirect calorimeter (metabolic cart) measurements of RMR

Method	Year Developed	Study Population	Equation
Harris-Benedict [4]	1918	N=239 (136 male, 103 female); mean age: males=27, females=32, mean BMI: males=21.4, females=24.4	Women: RMR[a] = 655.0955 + (9.5634 x W[b]) + (1.8496 x H[c]) – (4.6756 x A[d]) Men: RMR = 66.473 + (13.7516 x W) + (5.0033 x H) – (6.7550 x A)
WHO[19]	1981	Based on data of over 114 studies and 7,000 subjects, ~33% female	Age (years) / Sex / RMR (MJ/day) 18-30 / M / 0.063 (W) +2.896 F / 0.062 (W) +2.036 30-60 / M / 0.048 (W) +3.653 F / 0.034 (W) +3.538 >60 / M / 0.049 (W) +2.459 F / 0.038 (W) +2.755
Structure 4[1]	2013	Derived from a meta-analysis of 47 studies	RMR (male) =361+21.1(FFM[e])+4.77(FM[f]) RMR (female) =360+21.0(FFM)+4.68(FM)
Mifflin-St.Jeor[17]	1990	N=498 (251 male, 247 female), 264 normal weight, 234 obese	RMR = (9.99 x W) + (6.25 x H) – (4.92 x A) + (166 x sex (males, 1; females, 0)) - 161
Structure 11[1]	2013	Derived from a meta-analysis of 47 studies	RMR (male) =898-3.32(A)+14.3(FFM)+6.46(FM) RMR (female) =682-3.08(A)+12.9(FFM)+5.9(FM)
Structure 5[1]	2013	Derived from a meta-analysis of 47 studies	RMR (male) =503+18.3(FFM) RMR (female) =473+20.1(FFM)
Wang [18]	2000	Derived from 6 different studies	Equation 11: RMR =24.6 (FFM) +175
Nelson [5]	1992	N=212 (86 Male, 126 Female); 62% obese (males over 20% body fat, females over 30%)	RMR (kJ/day)=(108 x FFM) + (16.9 x FM)

[a] RMR=Resting metabolic rate (kcal/day); [b] W=weigh(kg); [c] H=height(m); [d] A=age(years); [e] FFM=fat-free mass(kg); [f] FM=fat mass(kg). Conversions: 1MJ= 238.85 kcal, 1kJ = 0.23885 kcal

Table 2. Demographic characteristics of the 30 male and female study participants testing the validity of resting metabolic rate prediction equations

	Male (n=15)	Female (n=15)	Total (n=30)
	mean ± SD	*mean ± SD*	*mean ± SD*
Age (years)	34.4 ± 13.1	42.0 ± 16.2	38.2 ± 14.9
Weight (kg)	88.5 ± 17.4	73.8 ± 13.7	81.1 ± 17.1
BMI (kg/m^2)[a]	28.2 ± 4.9	26.2 ± 4.1	27.2 ± 4.5
Body fat (%)[b]	26.2 ± 6.9	36.8 ± 6.4	31.5 ± 8.5
White race n (%)	14 (93.3)	15 (100)	29 (96.7)

SD: standard deviation

[a]Body mass index

[b]Calculated from dual x-ray absorptiometry as (body fat mass/body mass)*100

Table 3. Mean prediction bias and ± 2 standard deviation limits of agreement (LOA) for 24-hour resting metabolic rate (RMR) between predicted and metabolic cart-measured 24-hour RMR, and mean bias as a percentage difference between predicted and measured RMR, measured from 30 healthy adult participants

	Bias (24 hr Kcal)[a]	± 2 SD LOA	*p*	Bias (% measured RMR)[b]	*p*
	mean ± SD			*mean ± SD*	
Harris-Benedict[4]	-14 ± 193	-391, 364	0.99	-0.83 ± 1.80	0.65
WHO[19,c]	-25 ± 201	-522, 370	0.85	-0.16 ± 1.88	0.93
Structure 4[1,d]	-73 ± 184	-433, 288	0.03	2.50 ± 1.72	0.16
Mifflin-St.Jeor[17]	-96 ± 217	-522, 329	< 0.01	3.89 ± 1.85	0.04
Structure 11[1,d]	-133 ± 188	-502, 236	< 0.01	6.69 ± 1.58	< 0.01
Structure 5[1,d]	-176 ± 227	-620, 269	< 0.01	8.06 ± 1.93	< 0.01
Wang et al.[18]	-183 ± 169	-514, 149	< 0.01	9.71 ± 1.39	< 0.01
Nelson et al.[5]	-190 ± 160	-502, 123	< 0.01	10.41 ± 7.26	< 0.01

SD: standard deviation

[a]Bias as 24 hr Kcal = predicted RMR- measured RMR

[b]Bias as % RMR = 100* (predicted RMR- measured RMR)/measured RMR

[c]World Health Organization

[d]Population-specific meta-regression equation or 'structure' developed by Sabounchi et al.[1]

Table 4. Percentage of the 30 adult participants whose resting metabolic rate was either accurate, over-predicted, and under-predicted by each of the prediction equations[a]

	Accurate[b]	Over[c]	Under[d]
Harris-Benedict[4]	76.7	13.3	10.0
WHO[19,e]	66.7	13.3	20.0
Structure 4[1,f]	73.3	10.0	16.7
Mifflin-St.Jeor[17]	73.4	3.3	23.3
Structure 11[1, f]	70.0	3.3	26.7
Structure 5[1,f]	53.4	3.3	43.3
Wang et al.[18]	56.7	0	43.3
Nelson et al.[5]	53.3	0	46.7

[a]For each equation, data are expressed as % of total sample. Each row sums to 100%.

[b]Accurately predicted resting metabolic rate values fell within ±10% of the value obtained from indirect calorimetry (metabolic cart).

[c]Over-predicted resting metabolic rate values were ≥10% of the value obtained from indirect calorimetry.

[d]Under-predicted resting metabolic rate values were ≤-10% of the value obtained from indirect calorimetry.

[e]World Health Organization

[f]Population-specific meta-regression equation or 'structure' developed by Sabounchi et al.[1]