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A novel approach to predict 24-h energy expenditure based on hematologic volumes: development and validation of models comparable to Mifflin-St Jeor and body composition models

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Abstract

Background—Accurate prediction of 24-h energy expenditure (24EE) relies on knowing body composition, in particular fat-free mass (FFM), the largest determinant of 24EE. FFM is closely correlated with hematologic volumes: blood volume (BV), red cell mass (RCM), and plasma volume (PV). However, it is unknown whether predicted hematologic volumes, based on easily collected variables, may improve 24EE prediction.

Objective—The aim was to develop and validate equations to predict 24EE based on predicted BV, RCM, and PV and to compare the accuracy and agreement with models developed from FFM and with the Mifflin-St Jeor equation which is recommended for clinical use by the Academy of Nutrition and Dietetics.

Design—Participants had body composition measured by underwater weighing and 24EE by respiratory chamber. BV, RCM, and PV were calculated from 5 published equations.

Participants/setting—Native American and Caucasian men and women were studied (n = 351). Participants were healthy adults age 18–49 years from the Phoenix Metropolitan Area, AZ.

Main outcome measure—Accuracy to within $\pm 10\%$ of measured 24EE and agreement by Bland-Altman analysis.

Statistical analysis—Regression models to predict 24EE from hematologic and body-composition variables were developed in half the dataset and validated in the other half.

Results—Hematologic volumes were all strongly correlated with FFM in both men and women ($r = 0.94$). Whereas the accuracy of FFM alone was 69%, four hematologic volumes were individually more accurate (75–78%) in predicting 24EE. Equations based on hematologic volumes plus demographics had comparable mean prediction errors to that based on body composition plus demographics; though the Mifflin-St Jeor had modestly better mean prediction

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error, body-composition, hematologic, and Mifflin-St Jeor models all had similar accuracy (~80%).

Conclusion—Prediction equations based on hematologic volumes were developed, validated, and found to be comparable to Mifflin-St Jeor and body composition models in this population of healthy adults.

Keywords

Energy expenditure; hematology; body composition; indirect calorimetry; obesity

Introduction

Accurate prediction of energy expenditure (EE) is important for research and clinical care involving patients with overweight and obesity. In research, measurement of 24-hour energy expenditure (24EE) by whole-room indirect calorimetry is an important tool for studying obesity and metabolism.^{1,2} Although studies involving the respiratory chamber rely upon accurate prescription of energy intake (EI) to achieve a reasonable level of energy balance within the metabolic chamber, predicting the amount of food needed to match anticipated 24EE is challenging.³ Achieving energy balance is especially important in studies of substrate utilization as deviation from energy balance rapidly influences fuel selection (e.g. shift to fat over carbohydrate oxidation during underfeeding).⁴ Altered metabolism by under- or overfeeding undermines the assumptions for substrate utilization calculations.⁵ Methods for prescribing EI are heterogeneous and prediction of EI to achieve EB have included equations based upon anthropometrics (body mass index (BMI) and body weight), body composition factors such as fat-free mass (FFM) and fat mass (FM), and resting metabolic rate (RMR) adjusted for estimated physical activity level.^{3,4,6} RMR may be measured by metabolic cart or predicted based on FFM and FM.³ Improving energy balance has been achieved by using 24EE measurements using predicted EI and subsequently prescribing the measured 24hEE as EI in a second chamber.^{7,8} but adds time and expense. Adjustment of food provided at later times during the chamber, based on early EE measures, has been shown to improve accuracy, but requires alteration in meal schedule and percentage distribution.³

In clinical settings, recommending goals for dietary intake requires knowledge of individual energy needs.⁹ Although measurement by indirect calorimetry is ideal, this procedure is not feasible in most clinical settings and predicted energy needs can be used. For example, the 2016 position statement by the Academy of Nutrition and Dietetics⁹ recommended (in absence of indirect calorimetry to measure resting metabolic rate (RMR)) use of the Mifflin-St Jeor equation to estimate total energy needs,¹⁰ which is based on anthropometric and demographic variables to estimate RMR, multiplied by a physical activity factor.

FFM and EE are closely correlated but the physiological basis for this linear association between FFM and 24EE is uncertain since FFM is a heterogeneous compartment comprised of organs and tissues of different mass and of wide-ranging ability to consume oxygen.¹¹ However, there is an obligate relationship between oxygen consumption and supply,¹² and FFM is strongly related with total blood volume (BV), and closely related hematologic

compartments, red cell mass (RCM) and plasma volume (PV).¹³⁻¹⁷ The ratio of total body water (TBW) to FFM is about 0.73, a ratio that applies to humans and other mammals.¹⁸ The close relationship between hematologic volumes (BV, RCM, and PV) and FFM may be via TBW.^{17,19,20} Gold standard assessment of BV, RCM and PV requires injection of tracers²¹ and is therefore invasive. Prediction equations for BV, RCM, and PV have been developed which are based on easily obtainable factors such as age, sex, height, and weight.²²⁻²⁵ To the authors' knowledge, the association between predicted BV, RCM, and PV, and directly measured FFM or EE measures has not been evaluated.

The goals of this study were to assess (a) the degree to which these predicted hematologic volumes are associated with measured FFM and (b) the usefulness of these hematologic volumes for predicting 24EE. In order to evaluate the association between FFM and these predicted hematologic volumes, BV,^{22,24} RCM,^{23,25} and PV²⁵ were calculated using five published prediction equations in a group of healthy adults who also had body composition measured by underwater weighing (UWW). Regression models based on these estimated hematologic volumes were developed to predict 24EE and subsequently validated. The hypotheses, that these estimated hematologic volumes were able to predict 24EE better than models involving FFM, body composition, and the Mifflin-St Jeor equation, were evaluated.¹⁰

Materials and Methods

Participants, Body Composition, and Energy Expenditure

Written informed consent was obtained prior to participation. The study was approved by the Institutional Review Board of the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK). Volunteers were adults recruited from the Phoenix Metropolitan Area, AZ, and admitted to the clinical research unit who participated in an observational study investigating risk factors for obesity and type 2 diabetes as previously described^{2,26} and who had measurements of body composition by UWW and 24EE by whole-room indirect calorimetry (years 1985 to 1993). All participants were healthy by history, physical examination, and routine laboratory testing.

On admission, participants were provided a standard weight maintaining diet (daily kcal: 20% protein, 30% fat and 50% carbohydrates).²⁷ Height and weight were measured with the participant wearing light clothing. Body composition was assessed by UWW, with simultaneous determination of lung residual volume and percent body fat, FM, and FFM were calculated from the equation of Siri.²⁸ After at least 3 days on the weight-maintaining diet that started on admission, participants completed 24EE measurements by whole-room indirect calorimeter previously described in detail.²⁹ Participants were directed not to exercise (e.g. push-ups) while in the metabolic chamber, but may otherwise move freely about the chamber. Prescribed energy intake in the respiratory chamber was based on equations developed from previously measured 24EE (Men: $24\text{EI (kcal)} = 1238 + 14.1[\text{body weight (kg)}] - 5.7 [\text{BMI (kg/height}^2\text{)}]$; Women: $24\text{EI (kcal)} = 951 + 19.3 [\text{body weight (kg)}] - 18.2 [\text{BMI (kg/height}^2\text{)}]$).⁴ This prescribed energy intake in the chamber provided 4 balanced meals and is reduced approximately 80% to account for restricted physical activity

inside the chamber, compared with the weight maintaining diet provided to participants when they were outside the chamber.

Calculations for Hematologic Volumes

Five published prediction equations were used to calculate BV, RCM, and PV (Table 1). Two were chosen as they are the prediction equations recommended by the International Committee for Standardization in Haematology (RCM_{ICSH}, PV_{ICSH}).²⁵ Also selected were the formula for BV by Nadler et al. (BV_{Nadler})²² that is recommended by the National Blood Service of the United Kingdom to estimate BV to screen for blood donation eligibility,³⁰ and an estimate of red cell mass (RCM_{Pearson}) based on the Nadler et al BV equation.²³ Pre-operative estimate of BV is also important for patients undergoing surgery to guide fluid replacement. However, scaling based on actual body weight is problematic, particularly in patients with obesity,²⁴ prompting development of a BV formula (BV_{Lemmens}), based on BMI only and is more appropriate across a range of BMI.²⁴ BV_{Lemmens} was therefore included as well for the analysis.

Statistical Analysis

Of the 1109 metabolic chambers performed in the cohort, 421 chambers associated with 421 participants, who also underwent body composition measurements by underwater weighing, were selected. Only the first metabolic chamber for each participant was included (i.e. excluded repeat measurements of 24EE at subsequent visits). Analysis was restricted to those known to be Caucasian or Native American since there were few participants who identified as belonging to other races and to those with complete data ($n = 351$). Pearson correlations were used to determine associations between FFM and predicted hematologic volumes. To develop prediction equations for 24EE, the dataset was randomly divided in half into training and validation groups. Using the training dataset, linear regression models were developed from FFM and predicted BV, RCM, and PV as single determinants of 24EE. Moreover, to assess models involving FFM, BV, RCM and PV along with demographic factors, stepwise linear regression was employed. Two groups of models predicting 24EE were derived including 1) demographic variables and body composition (FFM and FM), and 2) demographic variables and hematologic volumes. Predicted 24EE values were calculated in the validation dataset. Agreement between predicted 24EE and measured 24EE was evaluated by paired t-test, Pearson correlation, and Bland-Altman analysis.³¹ Predicted 24EE within 10% of the measured 24EE were classified as accurate, as in previously published literature.³ Accuracy of models based on hematologic volumes was compared with accuracy of the FFM model or body composition model (i.e. with FFM and FM) by using the McNemar's test. Statistical significance was accepted at $p < 0.05$. Statistical analyses were performed using SAS software, version 9.3 (SAS Institute, Cary, NC, USA).

Results

A total of 351 participants were included (Table 2). Most participants were men (61%). Most participants were Native American (73%) while the remainder identified as Caucasian.

Correlation between hematologic volumes and fat-free mass

In correlation analysis, BV_{Nadler} , $BV_{Lemmens}$, RCM_{ICSH} , $RCM_{Pearson}$, and PV_{ICSH} were all strongly correlated with FFM ($r = 0.92$ for all hematologic volumes). The strong association remained when stratified by sex ($r = 0.94$ for all hematologic volumes) and by race ($r = 0.91$ for all hematologic volumes).

Development and validation of prediction equations for 24EE

FFM and predicted hematologic volumes as single determinants—Prediction equations for 24EE were developed by using the training dataset ($n = 176$) (i.e. half the dataset derived from a random sample of the full dataset). Equations were developed based on FFM and predicted hematologic volumes as single determinants of 24EE (Table 3). FFM alone explained 79.1% of the variance in 24EE. Compared with FFM, each hematologic volume individually accounted for a similar or slightly greater proportion of the total variance as FFM, with BV_{Nadler} , $BV_{Lemmens}$, $RCM_{Pearson}$, RCM_{ICSH} , and PV_{ICSH} explaining 83.1%, 78.8%, 83.7%, 79.4%, and 83.7%, respectively.

Prediction equations (Table 3) developed in the training dataset were evaluated in the other half of the dataset (validation dataset). Predicted 24EE by the FFM model ($r = 0.86$, $p < 0.001$) and by models involving BV_{Nadler} ($r = 0.87$, $p < 0.001$), $BV_{Lemmens}$ ($r = 0.84$, $p < 0.001$), $RCM_{Pearson}$ ($r = 0.86$, $p < 0.001$), RCM_{ICSH} ($r = 0.81$, $p < 0.001$), and PV_{ICSH} ($r = 0.86$, $p < 0.001$) were all highly correlated with measured 24EE (Table 4). Mean prediction error by hematologic models BV_{Nadler} (-29 ± 195 kcal/d), $BV_{Lemmens}$ (-34 ± 212 kcal/d), $RCM_{Pearson}$ (-27 ± 200 kcal/d), RCM_{ICSH} (-32 ± 231 kcal/d), and PV_{ICSH} (-28 ± 203 kcal/d) was not significantly different (p -value > 0.05) from mean prediction error by the body composition model (-29 ± 206 kcal/d) (Table 4). When compared with accuracy (i.e. predicted 24EE within $\pm 10\%$ of measured) of the FFM model (69%), prediction accuracies of BV_{Nadler} (75%, $p = 0.033$), $BV_{Lemmens}$ (78%, $p = 0.006$), $RCM_{Pearson}$ (77%, $p = 0.012$), and PV_{ICSH} (76%, $p = 0.029$) were significantly better (Table 4). Figure 1 shows agreement between measured and predicted 24EE by either the FFM model or by hematologic models using Bland-Altman plots. Visual assessment of the scatterplots (Figure 1) and the negative correlation coefficients in the FFM model ($r = -0.45$, $p < 0.001$) and in the hematologic models BV_{Nadler} ($r = -0.32$, $p < 0.001$), $BV_{Lemmens}$ ($r = -0.31$, $p < 0.001$), $RCM_{Pearson}$ ($r = -0.34$, $p < 0.001$), RCM_{ICSH} ($r = -0.33$, $p < 0.001$), and PV_{ICSH} ($r = -0.33$, $p < 0.001$) indicated that all the equations underestimated 24EE at higher average 24EE values.

Body composition and predicted hematologic volumes including demographics

—After evaluating FFM and hematologic volumes as single determinants of 24EE, prediction equations were developed, allowing for the inclusion of demographic variables, since they are routinely available. Since FM is available when FFM is measured, they were included together under the category of body composition. Two groups of equations were thus developed which involve: (a) body composition and demographics and (b) estimated hematologic volumes and demographics (Table 3). In the body composition model, FFM, FM, race, and sex were significant determinants of 24EE, together explaining 84.7% of the total variance. Prediction equations involving demographics and BV_{Nadler} , $BV_{Lemmens}$, $RCM_{Pearson}$, RCM_{ICSH} , and PV_{ICSH} explained a similar portion of the total

variance, 85.8%, 85.9%, 85.6%, 83.5%, and 85.5%, respectively. The y-intercepts for PV_{ICSH} in models as a single determinant and with demographics (Table 3) were about 90 kcal/d and not significantly different from zero.

Prediction equations (Table 3) developed in the training dataset were evaluated in the validation dataset. Predicted 24EE by the body composition model ($r = 0.89$, $p < 0.001$) and by models involving BV_{Nadler} ($r = 0.87$, $p < 0.001$), BV_{Lemmens} ($r = 0.87$, $p < 0.001$), RCM_{Pearson} ($r = 0.87$, $p < 0.001$), RCM_{ICSH} ($r = 0.84$, $p < 0.001$), and PV_{ICSH} ($r = 0.86$, $p < 0.001$) were all highly correlated with measured 24EE (Table 4). Mean prediction error by hematologic models BV_{Nadler} (-26 ± 192 kcal/d), BV_{Lemmens} (-29 ± 197 kcal/d), RCM_{Pearson} (-28 ± 198 kcal/d), RCM_{ICSH} (-39 ± 213 kcal/d), and PV_{ICSH} (-28 ± 202 kcal/d) was not significantly different (p -value > 0.05) from mean prediction error by the body composition model (-22 ± 184 kcal/d) (Table 4). When compared with accuracy (i.e. predicted 24EE within $\pm 10\%$ of measured) of the body composition model (81%), prediction accuracies of BV_{Nadler} (78%, $p = 0.23$), BV_{Lemmens} (78%, $p = 0.42$), RCM_{Pearson} (77%, $p = 0.18$), RCM_{ICSH} (77%, $p = 0.19$), and PV_{ICSH} (78%, $p = 0.42$) were similar (Table 4). Figure 2 shows agreement between measured and predicted 24EE by either the body composition model or by hematologic models using Bland-Altman plots. Visual assessment of the scatterplots (Figure 2) and the negative correlation coefficients in the body composition model ($r = -0.35$, $p < 0.001$) and in the hematologic models BV_{Nadler} ($r = -0.27$, $p < 0.001$), BV_{Lemmens} ($r = -0.26$, $p < 0.001$), RCM_{Pearson} ($r = -0.26$, $p < 0.001$), RCM_{ICSH} ($r = -0.25$, $p < 0.001$), and PV_{ICSH} ($r = -0.26$, $p < 0.001$), indicating that the equations underestimate 24EE at higher average 24EE.

Mifflin-St Jeor equation and predicted hematologic volumes including demographics—Since the Mifflin-St Jeor equation¹⁰ was recommended by the Academy of Nutrition and Dietetics for clinical use as the best equation for estimating RMR,⁹ models involving hematologic volumes and demographics were compared with this equation. A physical activity factor of 1.3 was used to account for activity within the metabolic chamber.^{3,32} Compared with models involving hematologic volumes and demographics, the mean error was less for the Mifflin-St Jeor equation (-0.15 ± 189 kcal/d, $p < 0.001$ for all comparisons) (Table 4). However, the Mifflin-St Jeor equation (79%) had accuracy similar to predictions equations involving hematologic volumes and demographics (77%-78%). The Mifflin-St Jeor equation also had less mean error than the mean error of the model involving body composition and demographics (-22 ± 184 kcal/d) ($p = 0.002$), but had similar accuracy (79% and 80%, respectively; $p = 0.53$).

Discussion

This study showed that predicted hematologic volumes are closely associated with FFM measured by a reference standard (i.e. UWW) of body composition. Models for predicting 24EE based on these hematologic volumes were derived and validated. Predicted BV, RCM, and PV in models as single determinants of 24EE were compared with models involving FFM alone. Individually, RCM_{ICSH} was found to be similarly accurate to FFM alone while the other four predicted hematologic volumes (BV_{Nadler}, BV_{Lemmens}, RCM_{Pearson}, and PV_{ICSH}) were more accurate. Models involving demographics plus predicted hematologic

volumes were derived and validated and compared with a model involving demographics plus body composition (including both FFM and FM). Models involving hematologic volumes were found to be as accurate as models involving body composition, indicating that prediction of energy expenditure can be done accurately without body composition measurements. Combining hematologic volumes with demographics also performed as well as, though not better than, the Mifflin-St Jeor equation as recommended for use (with a strong-evidence rating) by the Academy of Nutrition and Dietetics,⁹ if indirect calorimetry is not available. This study thus demonstrated a new approach to energy prediction that may be clinically useful that also does not rely on the additional equipment needed to measure body composition.

Although it is widely accepted that FFM is the single best determinant of 24EE, explaining most of the variance in energy expenditure between individuals,^{29,33} BV_{Nadler} , $RCM_{Pearson}$, and PV_{ICSH} individually were found to explain a larger portion of the variance in 24EE (83-84%) and were also more accurate (75-78%) than the model with FFM alone which explained 79.1% of the variance and was 69% accurate. The association between 24EE and estimated BV, RCM, and PV does not imply that these hematologic volumes are consuming oxygen directly. For example, red blood cells, containing hemoglobin but lacking mitochondria,³⁴ primarily function to carry oxygen and the RCM therefore is a reflection of oxygen carrying capacity. The PV compartment contains metabolic fuels for oxidation such as glucose and fatty acids and reflects the size of the pool actively transporting these fuels. Since BV is the sum of both the PV and RCM, the BV reflects circulatory pool of both metabolic fuel and oxygen. If efficient matching occurs between these circulatory compartments reflecting supply and tissue demand (under normal physiologic conditions), then these hematologic volumes may account for overall EE better than FFM. Measured BV, RCM, and PV has been shown to respond by expanding or contracting rapidly in response to increased physical activity or inactivity,³⁵ states which reflect higher and lower energy demands, suggesting that the body does sense energy needs and regulates these hematologic volumes accordingly. On the other hand, FFM alone may be an inferior predictor of 24EE because it represents a heterogeneous group of tissues and organs of varying metabolic rates.¹¹ It is also possible that there may be greater measurement error for FFM by UWW, compared with measurement error for height and weight which are used to calculate hematologic volumes, thus reducing the predictive ability of FFM.

Sex is a known determinant of 24EE in models involving body composition.³⁶ In the body composition model involving demographic variables, sex was a significant predictor of 24EE, with men having about 210 kcal/d greater 24EE than women. In parallel, men have greater hematologic volumes than women.^{37,38} Sex was not a significant predictor of 24EE in models involving $RCM_{Pearson}$ and PV_{ICSH} which suggest that these volumes may adequately account for differences in 24EE.

An advantage of using hematologic volume over body composition to predict 24EE is that the interpretation of the slope is more straightforward. Since FFM is a disparate group of tissues and organs,¹¹ the slope of FFM in prediction equations for 24EE does not allow for distinction between the metabolic rates of these tissues. On the other hand, BV, RCM, and PV are more well-defined compartments. In the BV equations, for every liter increase in BV,

there was an increase in 24EE of about 330-420 kcal/d. For RCM, there was an increase of about 740-890 kcal/d per liter increase in RCM. Similarly, there was an increase of about 730-740 kcal/d for every liter increase in PV.

Another perplexing finding of relying on FFM to predict 24EE (or resting energy expenditure) is the presence of a positive y-intercept which ranges from several hundred to about 800 depending on the study.^{3,11,29} Similarly, a significant non-zero y-intercept was present in the analysis using FFM based models. Although statistically valid, the biological interpretation of this non-zero intercept is uncertain as there is no EE at zero body mass. Others have approached this by compartmentalizing FFM into separate masses for different metabolic organs (e.g. brain, liver, heart, etc.) by imaging and this has been a way to reduce the y-intercept to near zero.^{11,39,40} Models with PV_{ICSH}, whether alone or adjusted for covariates (Table 3), had y-intercepts (about 90 kcal/d) that were very close to and not significantly different from zero which implies that there is no energy expenditure when PV_{ICSH} is extrapolated to zero.

A limitation of this study is that predicted as opposed to directly measured hematologic volumes were used to examine the relationship with FFM and 24EE.²¹ Since hematologic volumes were predicted and not measured, physiological interpretation of the hematologic volumes should be done cautiously, and definitive proof of the association between hematologic volumes and 24EE requires direct measurement of both. While it cannot be determined whether measured hematologic volumes would serve as better or equivalent predictors of 24EE, these published prediction equations for hematologic volumes were derived from more invasive methods and the associations with directly measured variables was very strong.

The study population, with its high percentage of Native American participants is unique and may not be generalizable to other populations. However, it is anticipated that these predicted hematologic volumes can be similarly predictive of 24EE in other laboratories since there was a very close association between FFM and predicted hematologic volumes. Moreover, these prediction equations were developed from a group of healthy ambulatory research volunteers with a wide range of adiposity and may not be generalizable to individuals who are ill or non-ambulatory. It is unknown whether using hematologic volumes to develop models in other populations (e.g. diseased) may improve prediction of energy expenditure compared with equations in current clinical use and is a potential direction for future research.

Although a reference method, UWW, was used to measure body composition, it is unclear how results would have changed if another method such as dual-energy X-ray absorptiometry (DXA) or bioelectrical impedance analysis (BIA) was used. FFM measured by DXA (another reference method) is highly correlated with FFM measured by UWW so it is anticipated that prediction of 24EE by DXA-based body composition models would be similar to prediction by UWW-based models. Although body composition measured by BIA is more readily available in clinical practice settings, BIA is considered less accurate than body composition assessment by DXA or UWW. Therefore, it is anticipated that prediction of 24EE by hematologic volumes would compare favorably if not better than BIA-based

models. However, body composition by either BIA or DXA was not available in the study participants so such models could not be evaluated.

In conclusion, prediction equations for BV, RCM, and PV were identified from the published literature and found to be highly associated with FFM. Equations from hematologic volumes and demographic factors were developed to predict 24EE measured by the metabolic chamber. These prediction equations for 24EE were validated and shown to perform comparably to models based on body composition and demographic variables and with an equation used to estimate energy needs recommended for use in clinical practice.

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Figure 1.

Bland-Altman plots showing agreement between measured and predicted 24-h energy expenditure by models with single predictor variables: (A) fat-free mass, (B) blood Volume_{Nadler}, (C) blood volume_{Lemmens}, (D) red cell mass_{Pearson}, (E) red cell mass_{ICSH}, and (F) plasma volume_{ICSH}. Dotted lines indicate mean difference and 95% limits of agreement. Solid line indicates the regression line and Pearson correlation was used. ICSH, International Committee for Standardization in Haematology.

Figure 2.

Bland-Altman plots showing agreement between measured and predicted 24-h energy expenditure by models with demographics plus either body composition (A) or hematologic volumes (B-F): (A) body composition, (B) blood volume_{Nadler}, (C) blood volume_{Lemmens}, (D) red cell mass_{Pearson}, (E) red cell mass_{ICSH}, and (F) plasma volume_{ICSH}. Dotted lines indicate mean difference and 95% limits of agreement. Solid line indicates the regression line and Pearson correlation was used. ICSH, International Committee for Standardization in Haematology.

Table 1
Prediction equations for blood volume, red cell mass, and plasma volume

Equation	
Blood volume	
Nadler, 1962 (22)	Male: $BV_{\text{Nadler}} = 0.3669 \times HT^3 + 0.03219 \times WT + 0.6041$ Female: $BV_{\text{Nadler}} = 0.3561 \times HT^3 + 0.03308 \times WT + 0.1833$
Lemmens, 2006 (24)	$BV_{\text{Lemmens}} = [70/\text{sqrt}(\text{BMI}/22)] \times WT / 1000$
Red cell mass	
Pearson, 1978 (23)	Male: $RCM_{\text{Pearson}} = BV_{\text{Nadler}} \times 0.47 \times 0.91$ Female: $RCM_{\text{Pearson}} = BV_{\text{Nadler}} \times 0.43 \times 0.91$
ICSH, 1995 (25)	Male: $RCM_{\text{ICSH}} = [(1486 \times S) - 825] / 1000$ Female: $RCM_{\text{ICSH}} = [(1.06 \times \text{Age}) + (822 \times S)] / 1000$
Plasma volume	
ICSH, 1995 (25)	Male: $PV_{\text{ICSH}} = (1578 \times S) / 1000$ Female: $PV_{\text{ICSH}} = (1395 \times S) / 1000$

BV, blood volume (l); HT, height (m); WT, weight (kg); sqrt, square root; BMI, body mass index (kg/m^2); RCM, red cell mass (l); ICSH, International Committee for Standardization in Hematology; PV, plasma volume (l); S, body surface area (m^2), $S = WT^{0.425} \times (HT/100)^{0.725} \times 0.007184$; Age (years)

Table 2
Characteristics of 341 healthy adult participants who had measurements of body composition and energy expenditure

Characteristic	M (n=214)	F (n=137)
Age (years), mean (SD)	27 (6)	27 (6)
Age range (years)	18-49	18-43
Race/ethnicity, n (%)		
Native American	161 (75)	94 (69)
Caucasian	53 (25)	43 (31)
Glucose regulation		
Normal, n (%)	154 (72)	77 (56)
Impaired, n (%)	60 (28)	60 (44)
Height (m), mean (SD)	1.72 (0.06)	1.61 (0.06)
Weight (kg), mean (SD)	98 (26)	92 (23)
Body mass index (kg/m²), mean (SD)	33 (8)	36 (9)
Body fat (%)	27 (8)	38 (7)
Fat-free mass (kg), mean (SD)	69 (12)	56 (10)
Fat mass (kg), mean (SD)	29 (15)	36 (14)
Blood volume-Nadler (l), mean (SD)	5.6 (0.9)	4.7 (0.8)
Blood volume-Lemmens (l), mean	5.6 (0.8)	5.0 (0.7)
Red cell mass-Pearson (l), mean (SD)	2.4 (0.4)	1.8 (0.3)
Red cell mass-ICSH (l), mean (SD)	2.3 (0.4)	1.6 (0.2)
Plasma volume-ICSH (l), mean (SD)	3.3 (0.4)	2.7 (0.3)
24-h energy expenditure (kcal/day)	2489 (360)	2107 (336)

M, male; F, Female

Table 3
Prediction equations for energy expenditure in a respiratory chamber

Model	Equation	r ²	p value
Fat-free mass as single determinant			
(1) 24EE = 723.01	+ 25.00 [FFM (kg)]	0.791	<0.001
Hematologic as single determinant			
(2) BV _{Nadler} 24EE = 476.10	+ 350.30 [BV _{Nadler} (liter)]	0.831	<0.001
(3) BV _{Lemmens} ^a 24EE = 98.84	+ 415.37 [BV _{Lemmens} (liter)]	0.788	<0.001
(4) RCM _{Pearson} 24EE = 675.63	+ 753.36 [RCM _{Pearson} (liter)]	0.837	<0.001
(5) RCM _{ICSH} 24EE = 821.69	+ 741.41 [RCM _{ICSH} (liter)]	0.794	<0.001
(6) PV _{ICSH} ^b 24EE = 87.99	+ 729.32 [PV _{ICSH} (liter)]	0.837	<0.001
Body composition plus demographics			
(7) 24EE = 892.27	+ 17.19 [FFM (kg)]	0.791	<0.001
	– 97.03 (Caucasian)	0.822	<0.001
	+ 7.40 [FM (kg)]	0.828	0.014
	+ 209.96 (Male)	0.847	< 0.001
Hematologic plus demographics			
(8) BV _{Nadler} 24EE = 552.88	+ 330.96 [BV _{Nadler} (liter)]	0.831	<0.001
	– 120.04 (Caucasian)	0.848	<0.001
	+ 97.27 (Male)	0.858	<0.001
(9) BV _{Lemmens} ^c 24EE = 229.81	+ 374.29 [BV _{Lemmens} (liter)]	0.788	<0.001
	– 127.23 (Caucasian)	0.839	<0.001
	+ 207.28 (Male)	0.859	0.021
(10) RCM _{Pearson} 24EE = 683.89	+ 764.85 [RCM _{Pearson} (liter)]	0.837	<0.001
	– 123.02 (Caucasian)	0.856	<0.001
(11) RCM _{ICSH} 24EE = 662.28	+ 888.77 [RCM _{ICSH} (liter)]	0.794	<0.001
	– 177.93 (Male)	0.815	<0.001
	– 125.01 (Caucasian)	0.835	<0.001
(12) PV _{ICSH} ^d 24EE = 88.83	+ 739.59 [PV _{ICSH} (liter)]	0.837	<0.001
	– 119.10 (Caucasian)	0.855	<0.001

Intercepts:

^a p = 0.27;

^b p = 0.25;

^c p = 0.003;

^d p = 0.22; all other intercepts p <0.001

24EE, 24-hour energy expenditure; FFM, fat-free mass; FM, fat mass; BV, blood volume; RCM, red cell mass; ICSS, International Committee for Standardization in Hematology; PV, plasma volume

Predictive abilities for measured 24-hour energy expenditure: comparison of models based on hematologic volumes with models based on body composition and the Mifflin-St Jeor equation ^a

Table 4

	FFM	Body composition	Mifflin-St Jeor	BV _{Nadler}	BV _{Lemmens}	RCM _{Pearson}	RC _{Mifflin}	PV _{ICSH}
Single determinants								
Predicted 24EE (kcal/d) ^b	2317 ± 305	-	-	2317 ± 334	2312 ± 333	2319 ± 330	2313 ± 322	2318 ± 330
Correlation (r) ^c	0.86	-	-	0.87	0.84	0.86	0.81	0.86
Mean error (kcal/d) ^b	-29 ± 206	-	-	-29 ± 195	-34 ± 212	-27 ± 200	-32 ± 231	-28 ± 203
Accuracy (%) ^e	69	-	-	75 ^f	78 ^f	77 ^f	73 ^d	76 ^f
Plus demographics								
Predicted 24EE (kcal/d) ^b	-	2324 ± 333	2346 ± 369	2319 ± 345	2317 ± 346	2318 ± 344	2306 ± 344	2318 ± 344
Correlation (r) ^c	-	0.89	0.88	0.87	0.87	0.87	0.84	0.86
Mean error (kcal/d) ^b	-	-22 ± 184	-0.15 ± 189	-26 ± 192 ^g	-29 ± 197 ^g	-28 ± 198 ^g	-39 ± 213 ^g	-28 ± 202 ^g
Accuracy (%) ^e	-	81	79	78 ^h	78 ^h	77 ^h	77 ^h	78 ^h

24EE, 24-hour energy expenditure; FFM, fat-free mass; BV, blood volume; RCM, red cell mass; ICSS, International Committee for Standardization in Hematology; PV, plasma volume

^aMeasured 24EE = 2346 ± 395;

^bMean ± standard deviation;

^cAll correlations $p < 0.001$;

^dNot significantly different from FFM model, $p > 0.05$;

^eAccuracy to within ± 10% of measured 24EE;

^fSignificantly different from FFM model, $p < 0.05$;

^gSignificantly different from Mifflin model, $p < 0.001$;

^hNot significantly different from models based on body composition or Mifflin equation, $p > 0.05$